IAPEN
Advancing Nutrition Care in India

CHOITHRAM
Hospital And Research Centre

Interburns
International Network for Training Education and Research in Burns

Life Long Learning
Initiative

Burn Nutrition Module

Edited by
Ms. Pratibha Sharma

**Advanced Training Workshop
on Nutrition Support in Burn Patients
12 October, 2013**

**Venue
Interburns Training Center (ITC)
Choithram Hospital And Research Centre
Manik Bagh Road, Indore, MP 452014**

CHOITHRAM
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Choithram Hospital & Research Centre is a Tertiary Care Apex Referral Medical Institute of Central India., dedicated to patient care with “Caring Touch”. The perfect balance between technology and humanity is crucial in healthcare and we put our best efforts to accomplish it by devotion, dedication and honest intentions of a specialized team of highly qualified individuals.

Our Mission and Vision

Choithram Hospital & Research Centre is a Tertiary Care Apex Referral Medical Institute of Central India., dedicated to patient care with “Caring Touch”. The perfect balance between technology and humanity is crucial in healthcare and we put our best efforts to accomplish it by devotion, dedication and honest intentions of a specialized team of highly qualified individuals.

Introduction of super specialty services in Healthcare Sector in Central India has emerged as our one of our major accomplishment in the last 3 decades of our service to the community. Today, the medical treatment is focused on preventive services, early diagnosis and keeping pace with it is not an easy task. CHRC works tirelessly to keep pace with International Standards in order to provide best, latest and efficient healthcare services to the community in the most cost effective manner. Faculties like Institute of Heart Sciences, Institute of Cancer Science, Institute of G.I. Sciences, Institute of Kidney Disorders, Institute of Paediatric & Neonatology etc. at CHRC, are all such additions which are highly appreciated by patient community throughout India.

To continue to serve the patient community and in order to minimize their discomfort by early and accurate diagnosis, methodical management, best curative efforts and rehabilitating them to fully fit in their desired activity level is our main objective. To live up to this challenge is not easy, particularly when there are no ready answers for many of the patient ailments. However, with an honest, devoted and dedicated approach, zeal, enthusiasm, innovation, care and devotion of highly qualified professionals; we strive to live up to the patient’s expectations. The effort has been recognized and many similar vision individuals have come together with us to help cure the illness and alleviate patient sufferings. The scientific battle with illness, sufferings and disability continues and so far it is our effort to provide complete solutions for patient illness and suffering at par with international standards at a reasonable cost.

Interburns Training Center (ITC)

The Interburns Training Center was formally started in January 2011 at Choithram Hospital and Research Center, Indore, India. The Choithram Hospital is a Private Charitable Trust 350 bedded Hospital with a 12 bedded Burn Unit admitting >220 acute burns and treating 1000 outpatients per year. The 4th Skin Bank in India was opened at the Burn Unit in February 2011.

The Interburns Training Center has been strategically placed at Indore because:

1. India has the highest global incidence of deaths from burn injuries

2. The Burn Unit has been run by a renowned burn care practitioner, Dr. Shobha Chamania since 1995 and has built an excellent burn care team and burncare model despite working within limited resources.

3. Burn training in the throughout the developing world is very limited. Until now most Trainees will visit the West for training and learn a large number of approaches and techniques not appropriate or possible for their local context. At the ITC comprehensive burn care can be taught and modelled which is relevant to the majority of contexts in Low Income Countries - and at a fraction of the cost.

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Interburns Training Center (ITC)

Saga begins from the motivation and whole hearted support of Late Shri Thakurdas Pagarani, He shared the painful demise of his mother due to burns and wanted to dedicate to society better care for the burns in her fond memory.

This service was started in 1988 with the objective of providing holistic burn care for patients in the city and neighboring regions as there was a crying need for a BURN CARE FACILITY.

Our burn unit has 12 beds for managing acute burns. Patient requiring critical care are managed in ICCU and PICU. Until now we have treated to more than 4500 burn patient and 10,000 outpatients. There is a multidisciplinary team dedicated to continuously work towards improving outcome. We offer early surgery and wound closure supported by the whole team of Surgeons, Physicians, anesthetists, nurses, dietician, physiotherapist and psychologist and paramedical staff.

Community services for increasing awareness on burn prevention are part of every member's responsibility. Burn support group and extended follow up service is provided for convalescent and discharged patient to look after the rehabilitation needs.

International achievement

Our burn unit is the Interburns (international network for training education and research in burns) Training Center. This center is being developed as a model training hub for all the members of the burn team and will cater to the needs of the Low and middle income countries. In future, interburns would like to duplicate these efforts in other developing countries. More details about Interburns can be found at their website: **www.interburns.org**'

Recent Activities

We have recently started a skin bank with support from Dutch Burn Foundation which is a great help in salvaging the life of a major burn victim. The skin bank is extremely indebted to the support of the social groups committed to raise awareness on organ donation. Muskan group and MK international eye bank need special mention here for their contribution and continued support. We have recently started a skin bank with support from Dutch Burn Foundation and Interburns.' Interburns funded the flights of the personnel who visited the Dutch Burn Foundation to develop the skin bank, at the request of Dr Shobha Chamania.

Fellowship Programs

This center has started a fellowship program from January 2011. The fellowship will be for one year which will give a good experience on managing all aspects of burns along with hands on training. The candidate will learn additional stuff on team management, designing a unit, infection control, community outreach and education on safety and first aid. He/she will be responsible for doing a research project and submitting the report at the end. Fellowship is also offered to the medical students wanting to do their electives in burns. This is for one month. This offers clinical experience and doing a small research project. Recent fellows at the ITC include burn care professionals from India, Nepal, and Uganda, with new fellows soon arriving from Tanzania and Afghanistan.'

International Network for Training, Education and Research in Burns

About Interburns

Interburns is an international network of expert burn care professionals seeking to transform the global provision of burn care in low and middle income countries (LMICs) through education, training, research and service delivery.

Our vision is a world where the enormous suffering, death and disability caused by global burn injuries have drastically decreased and every burns patient has access to the highest standards of burn care. We believe that all burns patients can receive good quality care despite limited resources. Our motto is 'tomorrow is too late', because urgent action is needed to address the terrible suffering burns cause to millions of people across the world.

Please support our work to transform care for burn patients across the world.

Our Strategic Aims

Training and Education
Create and deliver a comprehensive training and education programme for professional burn care teams, carers and the general public, which will radically transform burn injury prevention, standards, and patient outcomes.

Network Development
Build an international, multi-disciplinary network of highly motivated and expert medical volunteers to deliver high quality standards, research, training and education.

Research and Awareness
Develop a strong evidence base of research, data and literature on global burns injuries and existing burns care, in order to raise awareness of burns as a global health crisis at the local, national and international level.

Improving Burn Care Standards and Service Delivery
Set and implement the highest standards of burn care in low resource environments.

Organisational Growth and Development
Grow Interburns into a professional and effective non-profit organisation with the resources, strategy and operational capacity to transform global burns care.

Contact Interburns

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IAPEN
Advancing Nutrition Care in India

About The Indian Association for Parenteral and Enteral Nutrition

The Indian Association for Parenteral and Enteral Nutrition (IAPEN) is an organization in the field of parenteral and enteral nutrition and promotes basic research, clinical research, advanced education, organization of consensus statements about clinical care and quality control.

Aims and Goals

✍ To help ensure that those suffering from malnutrition or other nutritional problems are appropriately recognised and managed (adopted from BAPEN, UK)
✍ To help ensure that proper nutrition is supplied to children in orphanages, anganwadis and schools, students in hostels and pg accommodations, patients in hospitals, senior citizens in old age homes and customers in restaurants.

Objectives

1. To improve the nutritional care of people at risk of malnutrition and food adulteration whether in hospitals or in the community.

2. To improve the basic and advanced clinical research and to organize the consensus statements about clinical care and care quality control.

To support individual patients and groups needing nutritional intervention

✍ IAPEN will listen to patients'/carers' nutritional concerns and will act appropriately.
✍ IAPEN will lobby for patient centred policies relating to nutritional care.
✍ IAPEN will promote equity of access to nutritional care for all patients.

To establish a sound basis to enable realisation of the above objectives.

✍

✍ IAPEN will initiate and maintain regular meetings with the relevant government departments, specialist societies and other key stakeholders at national level.
✍ IAPEN will develop a robust financial structure.
✍ IAPEN will describe and implement a formal mechanism for raising funds for specific nutritional initiatives.
✍ IAPEN will identify a formal administrative infrastructure.

To raise awareness about IAPEN and its role in the healthcare agenda

✍ IAPEN will actively seek to increase its membership by recruiting new Individual Affiliates and new Associate Clinical Interest Groups.
✍ IAPEN will develop a commercially viable regular publication to share and disseminate good practice.
✍ IAPEN will develop effective links with other similar organizations while maintaining its singular position of expertise.
✍ IAPEN will establish regular meetings at regional level to encourage networking/information sharing.

To develop a robust and cohesive approach to information gathering about nutrition provision at national level and to identify/redress any gaps.

✍ IAPEN will support FOCUS initiatives targeted at identified areas of practice so that information can be collected and disseminated.
✍ IAPEN will produce regular reports and promote national standards of practice.

To identify which people are at risk of malnutrition

✍ IAPEN activities, related to under-nutrition, will be fully integrated in both hospital and community settings.
✍ IAPEN will try developing a systamatic protocol to fight malnutrition.
✍ IAPEN will ensure that its expertise and experience in the metabolic and practical management of patients with disease-related malnutrition is recognised and disseminated

Associate Organizations

BAPEN ESPEN KEPAN KLİNİK ENTERAL PARENTERAL NÜTRİSYON DERNEĞİ उत्तराखण्ड शासन NESPEN 'clinical nutrition and metabolism'

IAPEN

Advancing Nutrition Care in India

About The Indian Association for Parenteral and Enteral Nutrition

IAPEN is the additional link to the already existing chain consisting of American Society for Parenteral and Enteral Nutrition (ASPEN), European (ESPEN, BAPEN), Australian (AusPEN), Parenteral and Enteral Nutrition Society of Asia (PENSA) and South African (SASPEN) societies.

IAPEN is contacting nutritionists, dieticians, doctors, hospitals, Indian Medical Association (IMA), Indian society of Parenteral and Enteral Nutrition (ISPEN), Indian Dietetic Association (IDA), Nutrition Society of India (NSI), Animal Nutrition Society of India (ANSI), National Institute of Nutrition (NIN), Protein Foods and Nutrition Development Association of India (PFNDAI) and various government organizations to participate in development of nutritional quality control manual for hospitals, orphanages, old age homes, student hostels and anganwadis. IAPEN is also contacting international agencies (BAPEN, ASPEN etc.) for developing a systematic protocol to fight malnutrition in India.

IAPEN Activities

For Children

Children with autism, food allergies, growth and feeding problems, developmental delay, or learning, mood, and behavior problems often have undiagnosed nutrition problems. These have a powerful influence on the brain and whole body, especially during infancy and childhood.

IAPEN aims at developing a simple, systematic and economically feasible protocol for monitoring the nutritional intake in children.

Parents can join IAPEN to attend training programs on nutritional care. Parents can also interact with nutritional experts through online interface (Members only forum). Mobile number of nearest nutritional expert will also be provided, if required.

Organizations can join IAPEN for conducting training programs on nutrition. Nutritional intake in student hostels will also be monitored by IAPEN.

For Adults

IAPEN will visit orphanages and anganwadis for creating nutrition awareness. IAPEN will monitor the nutritional intake and give certification to the orphanages and anganwadis.

A certificate will be issued to eligible restaurants by IAPEN after verification of nutritional content in recipes. The restaurant name will be displayed in the members area and in the website.

Hospitals can join IAPEN for downloading information about nutritional intake of patients. Hospitals can submit queries in the members area. Mobile numbers and phone numbers of nutritional experts will also be provided, if required.

Note: IAPEN certification is a private certification by a Non-Governmental Organization. The certificate issued cannot be used similar to government licence. IAPEN is not liable for improper usage of its certificate.

For Elders

IAPEN will visit old age homes for creating nutrition awareness. IAPEN will monitor the nutritional intake and give certification to the old age homes.

IAPEN will issue a free certification to all old age homes. We will also formulate guidelines within their budget.

Old age homes can join IAPEN for receiving training on nutrition. We have also collected nutritious and cheap food recipes for elders.

Nutritional intake of elders suffering from various diseases will also be given to the members.

Scientific Committee Members

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For more details visit http://www.iapen.co.in

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Interburns

ADVANCED TRAINING WORKSHOP ON NUTRITION SUPPORT IN BURN PATIENTS

October 12th, 2013

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Dr. J. P. Majra, Hon President, The Indian Association for Parenteral and Enteral Nutrition, AP, India.

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Schedule of the Advanced Training Workshop
on
Nutrition Support in Burn Patients

October 12th, 2013

10.00 AM–10.30 AM: Registration
Inauguration and Release of Burn Nutrition Module

10.30 AM–10.45 AM: Tea Break

10.45 AM–12.15 AM: Pathophysiology and Nutrition Support in the Burn Patients: Fluid loss,Metabolic Response, Fluid Resuscitation and energy requirements, micro and macro nutrients support

12.15 AM–01.30 PM: Nutritional Assessments and Monitoring: Equations Used to Estimate Caloric, substrate, vitamin and trace element Requirements in Burned Patients

01.30 PM-02.00 PM: Lunch break

02.00 PM-03.30 PM: Administration routes, formula selection and calculations: Early enteral nutrition or Parenteral nutrition in acutely in burn patients

03.30 PM-03.45 PM: Case Studies, Skill Test and About IAPEN Life Long Learning

03.45 PM-04.00 PM: Hi - Tea and Valedictory and Certificate Distribution.

Life Long Learning Initiative

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Advanced Training Workshop
on
Nutrition Support in Burn Patients
October 12th, 2013

Module Contents

1. Basics in clinical nutrition: Nutritional support in burn patients by Meete Berger, Clinical Nutrition and Metabolism 4 (2009) e308–e312

2. Burns, metabolism and nutritional requirements by N. Mendonca Machado, A. Gragnani and L. Masako Ferreira, Nutricion Hospitalaria, 26(4) (2011) 692-700

3. Early enteral nutrition in acutely ill patients: A systematic review, Paul E. Marik, MD, FCCM; Gary P. Zaloga, MD, FCCM, Critical Care Medicine 29(12) (2001) Lippincott Williams & Wilkins

4. Nutrition in Burns: Galveston Contributions, Noe A. Rodriguez, Marc G. Jeschke, Felicia N. Williams, Lars-Peter Kamolz and David N. Herndon, Journal of Parenteral and Enteral Nutriition 35: 704 (2011), ASPEN, USA

Workshop Aim

Nutrition support represents a critical component in the care of the acutely burned patient. Management of nutritional demands mandates attention to the unique hypermetabolic state that results from major burn injury; this pathophysiology results in loss of lean body mass, increased fat accretion and protein wasting, and impaired wound healing. Historically, failure to address these problems in victims of major burn injury often resulted in a fatal degree of inanition and death from infection and heart failure.

The aim of this workshop on nutrition support in burn patient is to ameliorate and hopefully optimize the deranged metabolism resulting from burn injury and permit successful closure of the burn wound and resolution of the hypermetabolic state.

Objectives

Upon successful completion of this workshop, the candidate should be able:

– To know the principles of fluid resuscitation in burn patients.
– To be familiar with requirements for macronutrients and micronutrients in burn patients.
– To know the methods of administering nutrition in burn patients

e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 4 (2009) e308–e312

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Educational Paper

Basics in clinical nutrition: Nutritional support in burn patients

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Learning objectives

- To know the principles of fluid resuscitation in burn patients.
- To be familiar with requirements for macronutrients and micronutrients in burn patients.
- To know the methods of administering nutrition in burn patients.

The incidence of burn injuries has decreased in Western countries, but they remain a major problem throughout the world. Qualitatively, the metabolic responses of burn patients are similar to those of other trauma patients, although more severe, with a particularly intense acute phase. Burns also share similar additional morbidity from shock, acute respiratory distress syndrome, sepsis, and multiple organ failure, which occur in any severely injured patient. Burned patients are frequently managed in separate facilities, and have some specific medical characteristics:

- They suffer cutaneous exudative losses of fluids containing large quantities of protein, minerals and micronutrients, which cause acute deficiency syndromes.
- Venous access is more difficult due to the destruction of the skin at the puncture sites (higher risk of catheter related infection).
- The surface to repair is extensive and explains the requirement for prolonged nutritional support, which is rare in other trauma.
- Burn patients stay for much longer periods in intensive care units (ICU) compared with other trauma, and require more prolonged nutritional support.

E-mail address: espenjournals@espen.org (Editorial Office).

1. Pathophysiology

1.1. Fluid loss

In the early phase of burns >20% of body surface, there is a transient massive increase in capillary permeability, with an obligatory plasma loss from the intravascular space into the extravascular compartment, which causes the generalised oedema in major burns. The loss is proportional to the extent of injury. In addition there are water evaporative losses, and plasma weeps from the burned area (exudation). The permeability changes last for about 24 h, being maximal during the first 12 h and are mainly responsible for the extensive fluid requirements.

1.2. Metabolic response

The metabolic response to trauma is essentially biphasic, followed by a late recovery phase.

1. Immediately after injury, there is a period of haemodynamic instability with reduced tissue perfusion, and release of high levels of catecholamines. This initial phase has classically been called the «ebb phase». It is characterized by a lowered total oxygen consumption (VO_2), and low metabolic rate. Depending on the severity of injury and on the success of the haemodynamic resuscitation, it may be extremely short-lived and last a few hours, or persist for a few days depending on the severity of injury and the quality of resuscitation.
2. The ebb phase is progressively replaced by the «flow phase», characterized by high VO_2, elevated resting energy expenditure

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doi:10.1016/j.eclnm.2009.06.005

Table 1
Equations to estimate energy requirements.

Toronto	$EE = -4343 + (10.5 \times \%BSA\ burn) + (0.23 \times CI) + (0.84 \times EREE) + (114 \times T\ ^{\circ}C) - (4.5 \times days\ post\ injury)$
Harris–Benedict	TEE = EREE × activity factor × stress factor[a] where EREE = $M = 66.5 + (13.8 \times weight) + (5.0 \times height) - (6.8 \times age)$ $F = 655.1 + (9.6 \times weight) + (1.8 \times height) - (4.7 \times age)$

EREE = Harris–Benedict estimated REE; BSA = body surface area; TEE = total energy expenditure; CI = caloric intake during the previous day.
[a] Major surgery: 1.0–1.2, skeletal trauma: 1.2–1.5, major burn: 1.4–1.8.

(REE), elevated substrate flows and accelerated potassium and nitrogen losses. Visceral blood flow and splanchnic O_2 consumption increase, as do the total cardiac output and total VO_2. During this phase, the body's temperature is generally increased and central thermoregulation is shifted upward, especially in severe burns.

Literature of the 1970s reported increases in energy expenditure of 150–200% of REE, proportional to the severity and extent of the burn. Modern management has reduced this greatly, decreasing the need for very high energy intakes. The largest increase is during the first weeks, depending on the size of the burn, reverting slowly to normal thereafter.

Extensive protein losses occur from the skin surface. Skeletal protein catabolism is markedly increased: synthesis may be impaired well into the convalescent or anabolic phase of the illness. The synthesis of acute-phase reactants and some visceral proteins is increased. Net nitrogen balance is therefore negative. These changes may be blunted but not suppressed by good overall management and by nutritional support.

3. The recovery phase starts when the acute phase declines, and the burned surface is covered. This phase requires high levels of energy to cope with physical rehabilitation, and completion of wound healing (but less than during the first 2–6 weeks). After major burns, this phase may last up to 2 years.

2. Treatment

2.1. Fluid resuscitation

The most frequent formula used in the fluid resuscitation of burned patients is the Parkland formula, although this predictive volume is only indicative and may require adjustment in individual cases.

$$\text{Fluid requirement (ml)} = 4 \times \text{body weight (kg)} \times \text{total burn area (\%)}$$

One half of this fluid is administered as crystalloid over the first 8 h after injury and the rest over the next 16 h. Urinary output should remain >0.5 ml kg^{-1} h^{-1}. Since salt solutions are used for resuscitation, all formulae result in the delivery of approximately 0.5 mmol sodium per kilogram body weight per percent of burned area. Colloids may be started after about 12 h. Over the second 24 h, fluid requirements decrease to about 50%. From the third day the oedema fluid starts to be reabsorbed into the intravascular compartment, at which time the need for intravascular fluid support decreases further. Free water requirements may remain high, especially in the case of nursing on fluidised beds. Albumin should only be considered if the serum albumin drops below 15 g l^{-1}. Fluid shifts are extensive, and require patients to be weighed every day.

2.2. Non-nutritional measures

Resting energy expenditure can be influenced by other factors, including:

- nursing in a thermoneutral environment using radiant heat (28–31 °C),
- early debridement and grafting,
- management of fluids, infection, pain and anxiety,
- early enteral feeding,
- infections,
- pharmacological tools: administration of beta-blocking agents is one of the most successful in reducing REE, and carries limited risks. A recent trial carried out in severely burned children has shown that β-blockers may prove a safe way to reduce energy expenditure and protein catabolism. Hypermetabolism was partly reversed.

3. Nutrition

3.1. Energy requirements

The concept of hyperalimentation was developed for burn patients in the 1970s, and many formulae were devised to assess the energy requirements. The very frequently cited Curreri equation is a typical example: such formulae should not be used anymore. Actual measurements of REE by indirect calorimetry, however, usually show lower total energy requirements than that derived from the various formulae. The modern Toronto equation is the most accurate and useful, since it is the only one to take into account all the factors which affect requirements such as sex, weight, height, percentage of burn, fever, previous days' caloric intake and time elapsed since injury (Table 1).

According to modern literature, the REE in burned patients ranges from 1.3 to 1.5 times that estimated from the Harris–Benedict equation although, occasionally, slightly higher figures may occur. REE changes over time, with a peak lasting 2–6 weeks depending on burn severity and on complications. As both underfeeding and overfeeding do have deleterious consequences, accurate assessment of REE is desirable to adjust the individual caloric intake, particularly in patients with a prolonged and complicated course: in severely burned patients the access to indirect calorimetric determination or REE is recommended.

When an indirect calorimeter is unavailable, the Harris–Benedict equation adjusted for activity and stress remains the most classical tool. Clinically, an even simpler rough estimation can be used: it consists in setting the requirements at 30–35 kcal kg^{-1} day^{-1} for burns $<40\%$ BSA, and 35–50 kcal kg^{-1} day^{-1} in burns $\geq 40\%$ BSA depending on burn size. Daily weight determination allows the estimate of fluid balance in the short term and the monitoring of the adequacy of nutritional support in the medium to long term.

3.2. Proteins

Persistent muscle protein catabolism is a major problem in severely injured patients. Over the first 21 days after injury, critically ill trauma patients lose up to 16% of their total body protein content despite full nutritional support. During the first 10 days, close to two thirds of this protein loss comes from skeletal muscle, and from viscera thereafter.

Accurate nitrogen balances in burned patients are difficult because of the wound losses, which approximate to 10 g nitrogen per 10% burned BSA during the first week. They are so large in major burns that nutrition cannot compensate for them. Measurement of urinary nitrogen or urea nitrogen gives a useful reflection of the prevailing net catabolism. Nitrogen excretion may be as high as 30 g day^{-1} in severely burned patients compared to 2 g day^{-1} in fasted normal subjects. In a series of burned and injured patients, described by Larsson et al. in 1984, given 45–50 kcal kg^{-1} day^{-1} energy intake (high by modern standards), nitrogen balance improved up to a protein intake of 0.2 g kg^{-1} day^{-1} ($\approx$ to 1.25 g kg^{-1} day^{-1}), i.e. 2–3 times the minimum requirement for normal subjects. Further increases in nitrogen intake produced no further improvement in nitrogen balance. In practice we may give less energy and slightly more nitrogen than in this study.

In Europe, the current practice is to give 1.3–1.5 g protein kg^{-1} day^{-1} (0.2–0.25 g N kg^{-1} day^{-1}). Higher intakes are usually oxidized, contributing to the increased urea production rate rather than being used for anabolic purposes. As in health, nitrogen balance depends not only on the nitrogen or protein but also on the energy supply.

Plasma albumin levels decrease during the acute-phase response, although the fractional synthesis is increased. During the early phase after injury, serum concentrations are frequently below 20 g l^{-1}, due to increased capillary permeability and fluid dilution, as well as increased catabolism. Serum albumin remains between 25 and 30 g l^{-1} for many weeks, which is well tolerated. There is no rationale for providing albumin to burned patients on a systematic basis. Outcome studies carried out in severely burned children have shown no benefit from supplementation.

3.3. Lipids

Increased lipolysis occurs as part of the metabolic response to injury, giving high free fatty acid levels for oxidation and increasing glycerol release for gluconeogenesis. This increase results from elevated counter regulatory hormone levels (catecholamines and glucagon), along with decreased insulin sensitivity. It is recommended that fat supply should not exceed 30% of energy. According to a prospective randomised trial done by Garrel et al. (1995) normal fat supply may promote infectious complications, and lower proportions of fat (15% of the total calories) may lower infection rates. The type of fatty acid also appears unimportant.

3.4. Carbohydrates

Injury initiates a strong increase in endogenous glucose production and turnover. Glucose serves preferentially as a cellular fuel for healing wounds and inflamed tissues. Glucose oxidation rates increase to 130% above those of control subjects after trauma, and administration of glucose, even in large amounts, fails to suppress endogenous glucose production, gluconeogenesis, and protein breakdown.

Fatty liver from increased de novo lipogenesis is commonly observed in major burns. It probably results from hypercaloric feeding with excessive amounts of carbohydrate. Based on these considerations, it seems reasonable to avoid giving glucose at a rate in excess of 5 g kg^{-1} day^{-1}, and to use glucose–lipid mixtures for patients without lipid intolerance, due to the above mentioned maximal oxidizing capacity of glucose. This is even more important as it has been recently shown that tight glycaemic control $<$7 mmol l^{-1}, using insulin, reduces mortality in critically ill surgical patients. Optimal glycaemia has yet not been determined in burns although there is suggestive evidence that normoglycaemia is equally important in this group of patients. Insulin may have other beneficial effects as well, e.g. decreased protein catabolism and improved muscle protein synthesis.

3.5. Vitamins, trace elements and minerals

Burned patients suffer significant trace element deficiencies involving predominantly copper, iron, selenium and zinc. The patients lose biological fluids through cutaneous wound exudates, drains, and haemorrhage, which cause negative balances during the first week after injury. The exudative wound losses are so important that trace element depletion must be anticipated after major burns. The alterations in trace element metabolism are reflected in low plasma concentrations, which persist for many weeks after injury. The precise requirements for trace elements and vitamins have yet to be determined for burned patients, but all recent data agree that they are increased. The interpretation of low plasma levels is complicated by the acute-phase response, characterized by decreased plasma levels of iron, selenium and zinc, and increased copper. Supplementation with quantities of trace elements, matched to compensate the exudative losses, restores serum concentrations to some extent, as well as related enzymatic activities, such as glutathione peroxidase, which is dependent on selenium.

In addition to their nutritional functions, trace elements and vitamins have antioxidant functions, which are of great importance in burned patients, due to the increased free radical production observed after burn injury. Supplements should therefore be provided early, starting during the first hours after injury.

3.6. Micronutrients functions in major burns

- Vitamins A and E are involved in tissue repair.
- Fat-soluble vitamins D and K are stored in adipose tissue and are slowly depleted during prolonged diseases: there are no reports of deficiencies specific to burns.
- Water-soluble vitamins of the B complex are not stored in appreciable amounts and are rapidly depleted. Their requirements are increased, due to changes in carbohydrate metabolism (vitamin B_1).
- Vitamin C is important in collagen synthesis and also has an antioxidant effect. A total daily intake of 1–2 g is therefore recommended. According to recent studies, even this quantity may be insufficient during the early phase after burns, when the use of mega-doses may achieve a capillary leak stabilising effect.
- Copper, selenium and zinc are lost in large amounts through cutaneous exudates: depletion of body stores must be anticipated by early substitution in patients with major burns. Copper is of special importance in burns as collagen is dependent on it for maturation. Selenium is essential for glutathione peroxidase activity and zinc for immunity and cell replications.
- Magnesium and phosphorus losses through exudates are extensive and explain, to a large extent, the increased requirements in burns.

4. Nutracuetics in burns

4.1. Glutamine and arginine

Both amino acids are conditionally essential after injury. They improve the function of the gut mucosa as well as immune function, which may help to reduce septic complications in burned patients. Up to 30 g day^{-1} of glutamine and of arginine have been recommended, although there are, as yet, no conclusive data in burns. Nevertheless the requirements for both AA are likely to be

increased. A series of trials using a precursor of glutamine, ornithine α-ketoglutarate (OKG) have shown promising results in both animal and human settings, in terms of improved wound healing, and immunity.

4.2. ω-3 PUFA

These fatty acids are potential immunomodulatory and anti-inflammatory agents in a dose of up to 3–5 g day^{-1}. There are some data to show that these may in fact improve outcome. There are no specific burns trials. The role of other fatty acids remains to be established.

4.3. Antioxidants

These nutrients include vitamins C, E and β-carotene, selenium, and zinc. Supplementation has been assessed clinically with beneficial clinical results.

4.4. Immunomodulating diets (IMD)

The use of IMD is controversial in critically ill patients, including patients suffering major burns, who are frequently septic as well. There may be a role for these diets, which combine glutamine, arginine with other micronutrients, but conclusive trials are lacking. In our unit, IMD is used as a starting diet for a maximum of 7–10 days, and at a maximal volume of 1000 ml day^{-1} in combination with other polymeric diets with fibre and high nitrogen content. IMD is stopped as soon as there is evidence of infection, since it may have an adverse effect under these circumstances.

5. Route of administration

Burn injuries are a patient category in which the benefits of enteral nutrition are likely to be high, although the fluid shifts that occur in the shock-phase following severe burn cause significant oedema in the gut wall, and favour gastrointestinal paresis. Using the gastric route for enteral feeding during the first 24 h after injury, even in patients with major burns, is, however, associated with quite a high success rate. The practice, in Lausanne, is to use early enteral feeding, except when contraindicated by abdominal problems (abdominal or electrical injury).

5.1. The parenteral route

The intravenous route is the only way to deliver large amounts of micronutrients that are required during the first 2 weeks after injury. TPN is a second choice for nutritional support in burns, but may prove life saving to prevent or correct undernutrition due to insufficient energy delivery by the enteral route. Central venous access carries the risk of infection and sepsis. There is no place for peripheral nutrition in the burned patient. Excessive caloric and carbohydrate intakes, easily achieved with TPN and rarely with EN, should be avoided. Therefore, the daily monitoring of energy delivery is particularly important during TPN.

5.2. The enteral route

Enteral nutrition is preferred in burns as in other critically ill patients. Early enteral administration of nutrients can improve splanchnic perfusion (animal trials), blunt the hypermetabolic response, stimulate intestinal IgA production and maintain intestinal mucosal integrity. By the end of the first week after injury most of the patient's energy requirements should be supplied enterally.

Delayed gastric emptying is sometimes observed in burned patients, as a result of heavy sedation and analgesia, which these patients require. In severe cases, post-pyloric feeding solves these problems allowing nutritional support to be continued during long surgical procedures, thereby avoiding energy deficits. Careful monitoring is required to prevent pulmonary aspiration. Slow constant gastric or post-pyloric infusion is better tolerated than bolus administration. Gastric suction can be continued simultaneously with nasojejunal feeding.

Diarrhoea is a frequent complication of tube feeding. The causes of this complication are several, including antibiotics, excessive rate of administration of hyperosmolar feeds, etc. On the other hand, centres that use high doses of opiates for sedation observe severe constipation: our practice is to include the use of emolients from the 2nd day of injury in the feeding routine, and to use fibre containing diets.

Insisting on EN alone may cause insufficient energy delivery due to GI tolerance limitations and because many patients require repeated surgical interventions, with the nutritional consequences of repeated fasting, and the shortened time available for nutrient delivery. If nutritional requirements are not met using the enteral route, parenteral supplementary feeding may be given. The two techniques are complementary.

5.2.1. Enteral access

It is well known that the techniques people are used to, work best in their hands, but other methods of intestinal accesses should be kept in mind for the difficult case. A study by McDonald et al. (1991) performed in 106 burned patients showed that gastric feeding, initiated within 6 h of injury, was adequate in a large proportion of patients, although the caloric supply was significantly lower in the most severely burned patients >60% BSA. Nasogastric feeding tubes are the easiest to place, but are also easily displaced. Nasojejunal tubes are generally well tolerated, and allow feeding round the clock. Finally, with severe burns to the face, it may be very difficult, for surgical reasons, to leave a tube in the nostrils, and percutaneous endoscopic gastro- or jejunal feeding tubes (PEG or PEJ) may be an appropriate alternative. This technique carries its own risks, but has been used successfully in our unit in our most severely burned patients.

6. Summary

Patients with major burns have increased nutritional requirements. Energy requirements vary over time, with the largest increases being observed during the first weeks after injury. Enteral nutrition is the first choice, but may be supplemented by PN if nutrient intake is inadequate. Burned patients have increased trace element losses, which contribute to delayed recovery: this can be reversed by early intravenous supplementation. Weight changes and energy intakes should be monitored daily.

Conflict of interest

There is no conflict of interest.

Further reading

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Revisión

Burns, metabolism and nutritional requirements

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Abstract

Objectives: **To review the nutritional evaluation in burned patient, considering the literature descriptions of nutritional evaluation and energy requirements of these patients.**

Introduction: **Thermal injury is the traumatic event with the highest metabolic response in critically ill patients. Various mathematical formulas have been developed to estimate nutritional requirements in burned patient. Indirect Calorimetry is the only method considered gold standard for measuring caloric expenditure.**

Methods: **A survey of the literature and data was collected based on official data bases, LILACS, EMBASE and PubMed.**

Results: **The metabolic changes involved in hypermetabolism are designed to supply energy to support immune function, brain activity, wound healing, and preservation of body tissues. Body weight is considered the easiest indicator and perhaps the best to assess the nutritional status. The most common formulas utilized in these patients are the Curreri, Pennisi, Schofield, Ireton-Jones, Harris-Benedict and the ASPEN recommendations. For children is the Mayes and World Health Organization formula. The majority of mathematical formulas overestimate the nutritional needs. The regular use of Indirect Calorimetry supplies adequate nutritional support to the burn patient.**

Discussion: **The traditional nutritional evaluation considers anthropometry, biochemical markers and estimation of nutritional requirements. The weight provides a basis for decisions that are established in the clinical context. Classic parameters can be adapted to intensive care environment.**

Conclusions: **The use of Indirect Calorimetry is crucial to ensure the safety of the nutritional support of burn patients and this should be widely encouraged.**

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Key words: *Burns. Metabolism. Nutritional evaluation.*

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QUEMADURAS, EL METABOLISMO Y LOS REQUERIMIENTOS NUTRICIONALES

Resumen

Objetivos: **Revisar la evaluación nutricional del paciente quemado, considerando las descripciones bibliográficas de la evaluación nutricional y de los requerimientos energéticos de estos pacientes.**

Introducción: **la lesión térmica es el acontecimiento traumático con la mayor respuesta metabólica en los pacientes críticos. Se han desarrollado diversas fórmulas matemáticas para estimar los requerimientos nutricionales del paciente quemado. La calorimetría indirecta es el único método de referencia para medir el gasto calórico.**

Métodos: **se realizó una revisión bibliográfica y una recogida de datos a partir de las bases de datos oficiales LILACS, EMBASE y PubMed.**

Resultados: **Los cambios metabólicos que implican un hipermetabolismo están diseñados para aportar energía para mantener la función inmunitaria, la actividad cerebral y la curación de las heridas así como la conservación de los tejidos corporales. Se considera que el peso corporal es el indicador más sencillo y quizás el óptimo para evaluar el estado nutritivo. Las fórmulas más frecuentemente empleadas en estos pacientes son Curreri, Pennisi, Schofield, Ireton-Jones, Harris-Benedict y las recomendaciones de ASPEN. En los niños son la de Mayes y la de la Organización Mundial de la Salud. La mayoría de las fórmulas matemáticas sobreestiman las necesidades nutricionales. El uso habitual de la calorimetría indirecta proporciona un soporte nutricional adecuado en el paciente quemado.**

Discusión: **La evaluación nutricional tradicional considera la antropometría, los marcadores bioquímicos y la estimación de los requerimientos nutricionales. El peso proporciona la base para las decisiones que se establecen en el contexto clínico. Los parámetros clásicos pueden adaptarse al ambiente de los cuidados intensivos.**

Conclusiones: **el uso de la calorimetría indirecta es crucial para asegurar la seguridad del soporte nutricional de los pacientes quemados por lo que debería potenciarse.**

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Palabras clave: *Quemaduras. Metabolismo. Evaluación nutricional.*

Abbreviations:

TBSA: Total Body Surface Area.
ESPEN: European Society for Clinical Nutrition and Metabolism.
NRS: Nutritional Risk Screening.
ASPEN: American Society for Parenteral and Enteral Nutrition.
IC: Indirect Calorimetry.

Introduction

Thermal injury is the traumatic event with the highest metabolic response in critically ill patients.[1,2] This response is proportional to the size of the burn and damage continue years after the incident.[3] Pathophysiological changes induce an acute inflammatory response, peripheral resistance to insulin and immunodeficiency.[4,5]

The effect of continuous and prolonged secretion of cytokines on metabolism can lead to an unstable and hypercatabolic condition, causing multiple organ failure.[6]

Objective determination of nutritional needs should be accurately evaluated to ensure adequate nutrition for this condition. Knowledge of the patient's profile is essential to prevent under-nutrition or over-nutrition and to minimize the complications of nutritional support.[7]

Various mathematical formulas have been developed to estimate nutritional requirements in burned patient.[8] The objective of this study is to review the nutritional evaluation in burned patient, considering the literature descriptions of nutritional evaluation and energy requirements of these patients.

Methods and materials

A survey of the literature and data was collected utilizing the key words *burns, metabolism, nutritional evaluation* and *intensive care unit* based on official data bases from LILACS, EMBASE and PubMed.

Metabolic response to burns injury

The patient essentially exhibits two phases: the first is referred to the *ebb* stage, in which the patient shows a deficit in plasma volume and insulin levels, initial signs of shock, hypothermia, lowered oxygen consumption and a decrease in overall metabolic rate. After this, the body undergoes hormonal modifications and, the *ebb* phase evolves to the *flow* phase. This stage is characterized by an increased concentration of catabolic hormones regulating the metabolic response. An increase in heart rate, body temperature, calorie consumption, proteolysis and neoglycogenesis is observed.[9] These reactions result of metabolic events aimed at wound healing.[10]

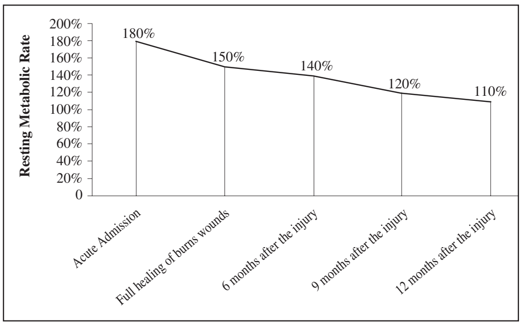

Fig. 1.—Resting metabolic rate of patients with more than 40% TBSA in thermal neutral temperature (33°C). Source: Herndon DN,Tompkins RG. Support of the metabolic response to burn injury. The Lancet. 2004;363:1895-902. Adapted.

Hypermetabolism begins at about the fifth post-burn day and persists for close to twenty-four months, causing loss of lean body mass, reduced bone density and muscle weakness, among other events.[11,12]

The intensive use of energy substrates predisposes the patient to malnutrition, which can cause a deficiency in the immune system, infections, an important nitrogen loss, delayed wound healing, prolonged hospital stay and mortality.[13,14]

The catabolic state is maintained by the inflammatory events activated by the damaged tissues. The cytokines released from these tissues transform the modified basal metabolism and keep it altered for long periods after acute trauma.[15]

Metabolic response in patients with more than 40% TBSA represents values above 100% of the resting metabolic rate.[10] (fig. 1).

Nutrition

Currently the concept that nutritional support plays an indisputable role in treating critically ill patient is well-accepted by scientific and health professional societies.[16] The metabolic changes involved in hypermetabolism are designed to supply energy to support immune function, brain activity, wound healing and preservation of body tissues.[17]

Tissue repair, accentuated and persistent muscle catabolism, and wound losses promote an increased protein needs after thermal injury. A clear recommendation is more problematic, although numerous investigators have discussed the increased protein needs of the thermally injured patient.[18]

The molecular mechanism of the hypermetabolic response to burn injury is not completely understood. Studies indicate that approximately 60% of the increased metabolic response to burn injury is attributable to an increased protein synthesis, gluconeogenesis, urea production and substrate cycling.[19]

Nutritional therapy aims: to offer favorable conditions for the establishment of the therapeutic plan, to

offer energy, fluids and nutrients in adequate quantities to maintain vital functions and homeostasis, recover the activity immune system, reduce the risks of overfeeding, ensure offers of protein and energy necessary to minimize the protein catabolism and nitrogen loss.[20]

Metabolic transformations involving nutrients

Exogenous protein, while capable of enhancing protein synthesis, cannot totally abate muscle protein breakdown despite high nitrogen intakes.[21] Protein breakdown may increase two to four times the usual levels, particularly in burn. Liver gluconeogenesis rises from 2.0 to 2.5 mg/kg body weight/min to 4.4 to 5.1 mg/kg body weight/min in the stressed patient.[17,22] Proteins play the most important role throughout the entire wound-healing process.[23]

Numerous studies have established that hypercatabolic and hypermetabolic states are associated with profound glutamine deprivation. A study conducted by Peng et al. (2005) found that when supplemented at a rate of 0.5 g/kg/day burned patients were capable of reversing the changes made during the burn.[24]

Hyperglycemia from metabolic perspective results from an increase in hepatic gluconeogenesis and a resistance to the action of insulin to clear glucose into muscle.[25]

Futile recycling of free fatty acids and triglycerides results of the enhanced lipolysis combined with fat oxidation.[23]

Nutritional evaluation

Assessment is used to identify patients who would benefit from nutritional support and suggests a design for that therapy.[26] In general, the same methods are used for other patients to conduct an assessment of nutritional status of critically ill patients, such as anthropometric and biochemical markers. However, nutritional assessment is limited in the burned patient.[27]

Most nutritional assessment tools available in a clinical setting are confounded by the physiological elements of the inflammatory response. Despite their limitations, many of markers of nutritional status when used collectively can help in daily monitoring of nutritional support.[21]

Table I
Nutritional Risk Screening (NRS)

Initial screening

	Yes	*No*
Is BMI < 20.5?		
Has the patient lost weight within the last 3 months?		
Has the patient had a reduced dietary intake in the last week?		
Is the patient severely ill? (e.g. in intensive therapy)		

Yes: If the answer is 'Yes' to any question, the screening in table II is performed.
No: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

Final screening

	Impaired nutritional status		*Severity of disease (E increase in requirements)*
Absent Score 0	Normal nutritional status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Wt loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild Score 1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. Chronic hemodialysis, diabetes, oncology
Moderate Score 2	Wt loss > 5% in 2 mths or BMI 18.5-20.5 + impaired general condition or Food intake 25-60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery* Stroke* Severe pneumonia, hematologic Malignancy
Severe Score 3	Wt loss >5% in 1 mth (>15% in 3 mths) or BMI >18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe Score 3	Head injury* Bone marrow transplantation* Intensive care patients (APACHE410)
Score		Score	**Total score:**

Score ≥ 3: the patient is nutritionally at-risk and a nutritional care plan is initiated.
Score < 3: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.
*indicates that a trial directly supports the categorization of patients with that diagnosis.

Table II
Description of peculiarities of burned patient that must be constantly monitored with the anthropometric assessment

Parameters	*Restrictions*	*Clinical Relevance*	*Method*	*Frequency*
Weight	It is affected by the presence of edema in burned patient and is a difficult variable to be monitored because of the patient's inability to walk by their clinical condition or bedridden for medical advice.	Provides monitoring of nutritional status of the patient while showing a simplified and general condition of the body compartments. This measure serves as a foundation of nutritional status and facilitates the monitoring during hospitalization.	Measuring with the aid of balance.	Biweekly during the acute phase and once a week during the convalescence.
Height	In some cases the patient may not want to cooperate or be unable to assist with measuring.	Assists in the investigation of nutritional status by BMI nutritional needs.	The measurement can be performed with the patient in a supine position with the aid of a fixed scale or tape measure properly.	On admission.
BMI (Body Mass Index)	May overestimate the nutritional status of patients with edema.	It is a noninvasive and practical tool for assessing nutritional status. The use of BMI is considered a good method of evaluation. Rates below 20 kg / m² are indicative of malnutrition and are associated with significant increase in mortality in different types of patient.	Mathematical formula: Weight/height². * Always consider the presence or absence of edema.	Weekly.
Evaluation of subcutaneous tissue	Impossible in patients with use of occlusive dressings and edema.	Constitutes a practical and noninvasive evaluation. Help in the verification of a deficiency status of long or short duration.	Symptomatic evaluation.	Weekly.
Evaluation of the Temporal Muscle	It may be impossible in patients with facial burns due to use of occlusive dressings or edema.	Constitutes a practical and noninvasive evaluation. Demonstrates the reduced intake of solid food and therefore calories and macronutrients. It is considered a physical sign of malnutrition.	Symptomatic evaluation.	Monthly.
Nutritional Risk	No specific restrictions.	Important tool for improving the nutritional therapy.	Questionnaire and verification of nutritional status.	During all the hospital stay.
%TBSA	Depends on the evaluation of plastic surgery.	Whereas energy expenditure is proportional to the length of the burn, the monitoring of wound healing must be done by the nutritionist to avoid overnutrition when the IC is not available. Practically speaking, the knowledge of %TBSA assists in monitoring and allows the application of predictive equations.	TBSA Diagram, adaptation scheme Lund-Browder.	Weekly.
Fasting	No specific restrictions.	Observation can be used as a tool to assess dietary intake and the clinical course of patients when analyzed together.	Verification of patient records and with the team.	Daily.
Estimation of energy requirements	Predictive equations tend to estimate the energy expenditure above or below the real, predisposing the patient to over-nutrition or under-nutrition.	Assists in the determination of nutritional therapy when the IC is not available.	Mathematical formulas described in the literature.	Weekly.
Measurement of nutritional needs with IC	The high equipment cost prevents the wide use of it in clinical practice.	It is considered the only valid method for determining the nutritional requirements by measuring the oxygen consumption and carbon dioxide excretion.	Specific exam.	Weekly
Assessment of nutritional intake	Depends on the patient's memory when it is made orally.	It is important for the detection of nitrogen and calorie balance. Assists in detecting eating disorders in which an excessive food restriction is adopted.	Interview with the patient completing the 24-hour recall or food record diary.	Daily.

Adaptation of:

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Nutritional risk is defined as "the chances of a better or worse outcome from disease or surgery according to actual or potential nutritional and metabolic status" by the European Society for Clinical Nutrition and Metabolism (ESPEN), Nutritional Risk Screening (NRS) 2002.[28,29] (table I).

According to the study by Hart et al. (2000) the five most significant variables in determining the magnitude of the catabolic response to severe burn were admission weight, percentage of TBSA burned, metabolic rate expressed as the percentage of the predicted energy expenditure, time from burn to the primary excision of the wound and burn sepsis.[30]

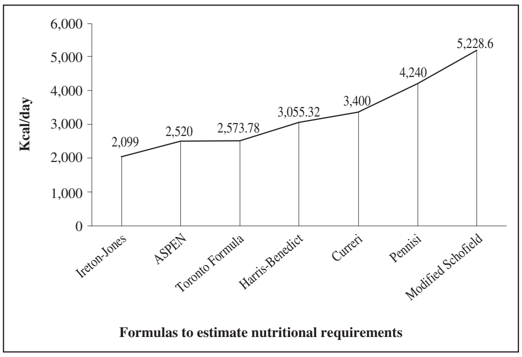

Fig. 2.—Distribution of nutritional requirements estimated by mathematical formulas for one adult burned patient. Electronic archive study, 2010.

Anthropometric variables

Body compartments and evolution of hydration status in burn patients invalidate anthropometric variables for nutritional evaluation.[31] Body weight is considered the easiest indicator and perhaps the best to assess the nutritional status.[32] Moreover, presence of edema are common.[27]

The anatomical point for the anthropometry measurements may be inaccessible and surgical procedures require days of bed rest. Semiologic analysis is important to detect the signs of depletion and some situations must be constantly monitored (table II).

Energy requirements

The size of the burn will proportionally influence the hypermetabolic response, inflammation, catabolism, changes in body composition, hormone production and organic dysfunction.[3,33]

The increase in energetic expenditure significantly contributes to the development of malnutrition and predicts that all adult patients with over 20% of TBSA must receive specific and individualized nutritional support.[34]

The majority of mathematical formulas overestimate the nutritional needs of burn patient.[11] It is difficult for a single formula to define individual nutritional needs with satisfactory precision, since all the factors involved in affecting metabolism are very complex. Predetermined equations to estimate energy expenditure are not recommended.[35,36]

Between 1970 and 1980 the most frequently used formula for estimating the nutritional needs of burn patients was developed by William Curreri.[37,38] In 1976, Pennisi created a more comprehensive formula, designed for adults and children, estimating both the energetic needs in calories and protein needs in grams.[39] Other formulas developed for critically ill and burn patients include Toronto,[40] Schofield,[41] Ireton-Jones,[42] Harris-Benedict,[43,44] and the American Society for Parenteral and Enteral Nutrition (ASPEN) recommendations.[45] The most widely formulas used in children are those of Harris and Benedict, Mayes and the World Health Organization[46] (table III).

A study by a group of researchers analyzed the accuracy of these formulas in children comparing caloric expenditure determined by IC. All the formulas overestimate the patient's caloric expenditure, predisposing him to over-nutrition.[47]

In order to compare the energy requirements suggested by the formulas most commonly used in adults, it was hypothesized a case of burn, and all formulas were employed. Hypothetically, was taken as reference for the use of formulas to a patient following conditions: 30 years old, weighing 72 kg, height 170cm, 40% of TBSA, bedridden, with eight days of burning, body temperature of 37ºC, breathing spontaneously and with average intake of 2.000 calories per day (fig. 2).

Over-nutrition predisposes the patient to hyperglycemia, overload of the respiratory system, steatosis and hyperosmolarity. When dealing with under-nutrition, the patient could suffer from malnutrition and subsequent reduction of immunocompetence, prolonged dependency on mechanical ventilation and delay in the healing processes, increased risk of infection, morbidity and mortality.[46]

In 1783, a study on the physiology of breathing – *Mémoire sur la Chaleur*, published by Lavoisier and Laplace for a periodical on the study of heat, generated the initial concepts of energy metabolism. The study explained the relationship between the inspired oxygen and the heat lost by the body.[48]

With respect to the study of energy metabolism, Indirect Calorimetry (IC) is the only research method considered gold standard for measuring caloric expenditure.[49] Identifying the patient's metabolic rate is essential to prevent deficits in energetic equilibrium. The regular use of IC supplies adequate nutritional support to the burn patient and is useful in the early detection of under-nutrition and over-nutrition.[50,51]

Due to its high cost, the use of IC for nutritional evaluation occurs mainly for research and few professionals have access to it. In the past 33 years, about 111 scientific articles reporting on burn injuries and IC have

Table III
Formulas for calculating approximate nutritional needs in burn cases. Electronic archive study, 2010

Author	*Gender*	*Formula*
Harris & Benedict BMR	Male Female	Estimated Energy Requirements: BMR x Activity factor x Injury factor 66 + (13.7 x weight in kg) + (5 x height in cm) - (6.8 x age) 665 + (9.6 x weight in kg) + (1.8 x height in cm) - (4.7 x age) *Activity factor* Confined to bed: 1.2 Minimal ambulation: 1.3 *Injury factor* < 20% TBSA: 1.5 20-40% TBSA: 1.6 > 40% TBSA: 1.7
Curreri	For all patients	Estimated Energy Requirements: (25 kcal x w) + (40 x %TBSA)
Pennisi	*Adults* Calories Protein	Estimated Energy Requirements: (20 x w) + (70 x %TBSA) (1 g x w) + (3g x %TBSA)
	Children Calories Protein	(60 kcal x w) + (35 Kcal x %TBSA) (3 g x w) + (1 g x %TBSA)
Toronto Formula	For all patients	Estimated Energy Requirements: [- 4343 + (10.5 x %TBSA) + (0.23 x kcals) + (0.84 x Harris Benedict) + (114 x T (°C)) - (4.5 x days post-burn)] x Activity Factors *Activity factors non-ventilated:* Confined to bed: 1.2 Minimal ambulation: 1.3 Moderate act, 1.4 *Ventilated-Depedent:* 1.2
Modified Schofield	Men	Estimated Energy Requirements: BMR x Injury factor 10-18 yrs = (0.074 x w) + 2.754 18-30 yrs = (0.063 x w) + 2.896 30-60 yrs = (0.048 x w) + 3.653 60 yrs = (0.049 x w) + 2.459
	Women	10-18 yrs = (0.056 x w) + 2.898 18-30 yrs = (0.062 x w) + 2.036 30-60 yrs = (0.034 x w) + 3.538 > 60 yrs = (0.038 x w) + 2.755 *Injury Factors:* < 10% TBSA = 1.2 11-20% TBSA = 1.3 21-30% TBSA = 1.5 31-50% TBSA = 1.8 > 50% TBSA = 2.0
ASPEN	For all patients	25 a 35 kcal/kg/day
Ireton–Jones Formula	For spontaneously breathing patients	Estimated Energy Requirements: 629 – (11 x yrs) + (25 x w) – (609 x O)
	Ventilated-Dependent	1784 – (11 x yrs) + (25 x w) + (244 x S) +(239 x t) + (804 x B)
WHO	For Children Male < 3 years Male 3 to 10 years	 (60.9 x weight in kg) – 54 (22.7 x weight in kg) + 495
	Female < 3 years Female 3 to 10 years	(61 x weight in kg) – 51 (22.5 x weight in kg) + 499
Mayes	For Children Male & Female < 3 years Male & Female 3 to 10 years	Estimated Energy Requirements: 108 + (68 x weight in kg) + (3.9 x %TBSA) 818 + (37.4 x weight in kg) + (9.3 x %TBSA)

Kcals: calorie intake in past 24 hours;
Harris Benedict: basal requirements in calories using the Harris Benedict formula with no stress factors or activity factors;
T: body temperature in degree Celsius;
Days post burn: the number of days after the burn injury is sustained using the day itself as day zero;
w: weight in kg;
yrs: age in years;
S: Male = 1 / Female = 0
t : trauma present:1 / No trauma present :0
O: presence of obesity > 30% above IBW: 1 / absent: 0
B: burn present = 1 / No burn present = 0

been published. The rate of publications over the last three decades follows an irregular pattern.

Nutritional support

The American College of Chest Physicians suggests that enteral nutrition should be initiated as soon as possible after resuscitation.[52] Burn patients frequently receive inadequate nutrition, initially because of hemodynamic instability and paralytic ileus. Eventually, nutrition is still inadequate due to required fasting for surgical procedures or diagnostic exams, the difficulty in chewing solid foods because of facial burns and due to anorexia and vomiting.[53]

The introduction of nutritional support cannot suppress hypermetabolic and hypercatabolic responses produced by a burn. Nevertheless, simply providing enteral nutrients in the first 24 hours postburn, reduces the caloric deficit.[54]

A study designed to compare the benefits of enteral nutrition when provided in different amounts was verified that the mortality of patients in the group receiving enteral nutrition in the proportion of 30 kcal/kg/day or more had lower mortality rates.[32,55]

In general rule critically ill adults require around 2 g of protein/kg/day or approximately 15% to 20% of total caloric intake in 24 hours.[56] The nutrients often used for Pharmacological nutrition in burned patients are glutamine, arginine and omega-3. These components, when supplied in quantities 2-7 times higher than those commonly eaten by healthy people, appear to have a beneficial effect on the pathophysiological changes induced by burns.[57]

Discussion

Nutritional support has become a major focus in the care of severely burned patients to overcome clinical events.[55] Malnutrition is an increasing problem in critically ill adults and can have a profound impact on outcomes. Given the ongoing challenges associated with nutrition screening, assessment, and support processes, this situation is perhaps not surprising. There is an unacceptably high prevalence of malnutrition in critically ill adults.[52]

Nutrition support may reduce morbidity and mortality after severe thermal injury, but excessive caloric and protein intakes cannot overcome the catabolic response to critical illness.[18]

Some patients do not exhibit the expected hypermetabolic response from their wounds. There are other individual factors that interfere with this response and advance the patient's progress to hypometabolism. The chief factors responsible for this unusual response are: the use of analgesia and sedatives, the presence of malnutrition, hypothyroidism, shock or hemodynamic instability, cellular bio-energetic failure, hypothermia and advanced hepatitis.[58]

This unusual response of some patient's causes an increase in the risk of developing clinical complications related to over-nutrition, because this picture is "masked" by typical hypermetabolism of burn patients. Accurate determination of resting energy expenditure is necessary in patients receiving nutritional support to ensure that their energy needs are met and to avoid the complications associated with over or underfeeding.[59]

Determining nutritional needs in burns becomes a challenge for nutritionists. The valorization of metabolic aspects of critical ill patient should be promoted with the inclusion of IC equipment. Nutritional evaluation should include a specific investigation, considering the clinical condition and patient's exposure to situations that may interfere with nutritional support.

In clinical practice, the burned patient is constantly exposed to periods of fasting, mostly due execution of examinations or surgical procedures. However, what differs this from other patients in intensive care is the constant need to make bandages. The frequency of these procedures can be daily and also require fasting. Moreover, it is widely described in literature that some inflammatory markers induced anorexia in patients submitted to metabolic stress.[60,61]

Keeping patients "fasted" to avoid aspiration complications when attempting extubation and a variety of other reasons generally delay enteral feeding. Several studies and reviews have shown that only about 75% of prescribed nutrients are actually delivered, with substantial variability.[62]

Even in a simple fasting, as a prolonged fasting, the body of an average adult loses about 60 to 70 g of protein (240 to 280 g of muscle tissue) per day. In severe trauma or sepsis, this loss can reach 150 to 200 g (600 to 1,000 g of muscle tissue) per day.[27]

The constant development of nutritional assessment reveals a promising future for the discipline. The results of these investigations will allow professionals in the field to broaden knowledge and devise new treatment strategies, improving the quality of care. Nutrition occupies a central role in our lives and for this reason it should be approached seriously, especially in pathological states.

Conclusion

There are lists of possible markers for nutritional assessment, but a minimum set of standards should be established. The use of IC is crucial to ensuring the safety of the nutritional support of burn patients and this should be widely encouraged.

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Early enteral nutrition in acutely ill patients: A systematic review

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Objective: **To evaluate the effect of early enteral nutrition on the outcome of critically ill and injured patients.**

Data Sources: **MEDLINE, citation review of relevant primary and review articles, personal files, and contact with expert informants.**

Study Selection: **Randomized, controlled studies that compared early with delayed enteral nutrition in hospitalized adult postoperative, trauma, head-injured, burn, or medical intensive care unit (ICU) patients. From 161 articles screened, 27 were identified as randomized, controlled trials comparing early with delayed enteral nutrition and were included for data extraction. Of these, 12 were excluded. None of the studies included medical ICU patients.**

Data Extraction: **Fifteen studies containing 753 subjects were analyzed. Descriptive and outcome data were extracted independently from the articles by the two reviewers. Main outcome measures were infections, noninfectious complications, length of hospital stay, and mortality. The meta-analysis was performed using the random effects model.**

Data Synthesis: **Early enteral nutrition was associated with a significantly lower incidence of infections (relative risk reduction, 0.45; 95% confidence interval, 0.30–0.66; p = .00006; test for heterogeneity, p = .049) and a reduced length of hospital stay (mean reduction of 2.2 days; 95% confidence interval, 0.81–3.63 days; p = .004; test for heterogeneity, p = .0012). There were no significant differences in mortality or noninfectious complications between the two groups of patients.**

Conclusions: **The results of this meta-analysis support the experimental data demonstrating the benefit of the early initiation of enteral nutrition. The results of this meta-analysis must, however, be interpreted with some caution because of the significant heterogeneity between studies. (Crit Care Med 2001; 29:2264–2270)**

KEY WORDS: meta-analysis; early enteral nutrition; delayed enteral nutrition; jejunostomy; postoperative; trauma; burns; intensive care unit; critical care

During the last two decades, nutritional support has emerged as a vital component of the management of critically ill patients. Nutrition supplies vital cell substrates, antioxidants, vitamins, and minerals that optimize recovery from illness. The hazards of parenteral nutrition compared with enteral nutrition (i.e., immune compromise, increased infections, increased complications, increased mortality in some patient subsets) are now clearly established and favor the use of enteral nutrition (1–9). Specialized immune-enhancing nutritional formulations have been developed, and these diets have been demonstrated to decrease indexes of inflammation, to improve cell-mediated immunity, to decrease organ failure and intensive care unit (ICU) complications, and to reduce ventilator and ICU days (10–19). The optimal time to start nutritional support is, however, an important and unresolved issue.

Many critically ill, injured, and postoperative patients develop gastroparesis, which limits the ability to tolerate gastric feeding (20, 21). Furthermore, these patients frequently have diminished or absent bowel sounds that are incorrectly interpreted to indicate that the small bowel is "not working." There is also the fear that early enteral feeding will result in aspiration and worsened clinical outcome. Finally, some believe that patients can tolerate 5–7 days of starvation without detrimental clinical effects. As a result, enteral nutrition is frequently withheld for 5–7 days until the return of gastric emptying and bowel sounds. However, it is now recognized that small-bowel function and the ability to absorb nutrients remains intact, despite critical illness, the presence of gastroparesis, and absent bowel sounds. In patients unable to tolerate gastric feeding, access to the small bowel can be obtained by small-bowel feeding tubes placed at the bedside, during surgery, endoscopically, or percutaneously.

It has been suggested that early enteral feeding may reduce septic and nonseptic complications and improve the outcome of the critically ill and injured patient (22, 23). There are several mechanisms whereby early enteral nutrition may improve patient outcome. Early enteral nutrition (as opposed to delayed enteral nutrition) has been demonstrated to improve nitrogen balance, wound healing, and host immune function, to augment cellular antioxidant systems, to decrease the hypermetabolic response to tissue injury, and to preserve intestinal mucosal integrity (i.e., maintain mucosal immunity, prevent increased mucosal permeability, and decrease bacterial translocation) (22, 24–29). Although the benefits of early nutritional support have been demonstrated at the cellular and tissue level and in animal studies of critical illness, the effect on patient morbidity and mortality has been less clear. Many studies demonstrated an improvement in one or more outcome variables. However, the studies were underpowered and, hence, the differences between early and delayed feeding groups were not always significant (22, 23). Furthermore, the magnitude of the treatment effect remains unknown (22, 23). We, therefore, performed a meta-analysis of available studies that compared early with delayed enteral nutrition to provide an estimate of the treatment effect of early enteral nutrition on patient outcome.

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METHODS

Identification of Trials. Our aim was to identify all relevant randomized, controlled trials that compared early with delayed enteral nutrition. A randomized, controlled trial was defined as a trial in which subjects were assigned prospectively to one of two interventions by random allocation. We used a multiple-method approach to identify relevant studies for this review. A computerized literature search of the National Library of Medicine's MEDLINE from 1966 to August 2000 was conducted using the following search terms: "enteral nutrition (explode)" *and* "early or immediate or delayed" *and* "randomized controlled trials (publication type)" *or* "controlled clinical trials" *or* "clinical trials, randomized." Bibliographies of all selected articles and review articles that included information on enteral nutrition were reviewed for other relevant articles. In addition, each author reviewed his personal files and contacted experts in the field. This search strategy was done iteratively, until no new potential, randomized, controlled trial citations were found on review of the reference lists of retrieved articles.

Study Selection and Data Extraction. The following selection criteria were used to identify published studies for inclusion in this analysis: a) study design: randomized clinical trial; b) population: hospitalized adult postoperative, trauma, head-injured, burn, or medical ICU patients; c) intervention: early vs. late/delayed institution of enteral nutrition; and d) outcome variables: at least one of the following primary outcome variables: the number of infections, total number of noninfectious complications, length of hospital stay (LOS), and hospital mortality. For the purposes of this meta-analysis, early enteral nutrition was defined as the initiation of enteral feeds within 36 hrs of admission to the hospital or within 36 hrs of surgery. Delayed enteral nutrition was defined as nutritional support that was initiated after 36 hrs of admission to the hospital or after 36 hrs of surgery. Study selection and data abstraction was conducted independently by the two investigators.

Data Analysis. Infections, complications, and mortality were treated as binary variables. LOS was treated as a continuous variable. The data analysis was performed using the random effects model with meta-analysis software (RevMan 4.1, Cochrane Collaboration, Oxford, UK). The relative risk and continuous data outcomes are presented with 95% confidence intervals. When authors reported standard deviations (SD), we used them directly. When SD were not available, we computed them from the observed mean differences (either differences in changes or absolute readings) and the test statistics. When the tests' statistics were not available, given a p value, we computed the corresponding test statistic from tables for the normal distribution. Subgroup analyses were performed on each of the postoperative, trauma, head-injured, and burn groups for each outcome variable. We found no studies that met the inclusion criteria for medical ICU patients. These subgroups were chosen because they reflect the main clinical populations included in the trials. We tested heterogeneity between trials with chi-square tests, with $p \leq .05$ indicating significant heterogeneity (30).

RESULTS

From 161 articles screened, 27 were identified as randomized controlled trials comparing early with delayed enteral nutrition, and were included for data extraction. Of these, 12 were excluded; the remaining 15 trials (31–45) were included in this meta-analysis. Articles were excluded for the following reasons: nocturnal protein supplementation was compared with control (n = 5) (46–50); enteral nutrition was delayed for >36 hrs in the early feeding group, with feeding delayed for up to 57, 60, and 96 hrs (n = 3) (51–53); the control group was not randomized (n = 1) (54); pediatric patients were included (n = 2) (55, 56); and patients in the treatment group received parenteral nutrition in addition to enteral nutrition (n = 1) (26). Overall, 753 patients were enrolled in the included studies. In none of the studies was their crossover to the other arm of the study. It is important to note that no studies of medical ICU patients were found. A summary of the studies, including the differences in caloric intake, is presented in Table 1. The study outcome data are presented in Table 2.

Infections. Information on the incidence of infections was available for 12 of the 15 (80%) studies and included 603 patients. Overall, there was a significantly lower risk of infection in the patients who received early enteral nutrition (relative risk of 0.45; 95% confidence interval [CI], 0.30–0.66; p = .00006) (Fig. 1). Infectious complication occurred in 19% of the early nutritional group as compared with 41% in the delayed group. The test for heterogeneity between the studies just reached statistical significance (p = .049).

Noninfectious Complications. Information on the incidence of noninfectious complications was available for 9 of the 15 studies (60%). The incidence of noninfectious complications was 33% in the early group compared with 38% in the delayed group; this difference was not significant (relative risk, 0.82; 95% CI, 0.56–1.19) (Fig. 2).

Length of Hospital Stay. Information on LOS was available for 12 of the 15 studies (80%). The LOS was significantly shorter in the early nutrition group (p = .0012; mean reduction of 2.2 days; 95% CI, 0.81–3.63 days) (Fig. 3). The reduction in LOS was most marked in the trauma/head injured/burn patients (4.04 days with 95% CI of 1.28–6.81days; p = .004). There was, however, significant heterogeneity between studies (chi-square = 30.7; p = .0012).

Mortality. Information on hospital mortality was available for only 6 of the 15 (40%) studies. The mortality was 8% in the early group and 11.5% in the delayed nutrition group; this difference was not significant (relative risk, 0.74; 95% CI, 0.37–1.48) (Fig. 4).

DISCUSSION

This systematic review is stronger than previous overviews of this topic in its adherence to strict methodologic criteria (22, 23). We used explicit inclusion and exclusion criteria, performed a comprehensive literature search, assessed the validity of eligible studies, and conducted a rigorous data analysis. This meta-analysis demonstrates a benefit of early enteral nutrition in reducing episodes of infection and LOS. There was, however, significant heterogeneity among the results of the primary studies. Nevertheless, we proceeded with the meta-analysis despite the presence of heterogeneity, because, short of a large randomized, controlled, and blinded study, our results provide the best guide for clinicians to judge the magnitude of the treatment effect of early enteral nutrition. Although the random effects model results in more conservative 95% CI, because of the significant heterogeneity among the studies, the results of this meta-analysis should be interpreted with some caution. Furthermore, as with any meta-analysis, there may be bias as it is easier to publish a study that shows a difference between the experimental and control group than a negative study (publication bias) (57).

When conducting a systematic review, heterogeneity (major differences in the apparent effect of the interventions across studies) is often found; if present, it should be explained (30). Heterogeneity between studies may be the result of the play of chance, the methodologic quality of the studies, differences in the patient populations, differences in study design, and unconcealed randomization

Table 1. Summary of nutritional support of the studies included in meta-analysis

Date	Author	n	Study Protocol	Formula	Caloric Intake (kcal) or % of Goal; Control vs Intervention (Mean ± SD)	
Abdominal surgery						
1979	Sagar (31)	30	SBT <24 hrs	Elemental diet	Day 2	300 ± 20 vs 1100 ± 100
1991	Schroeder (32)	32	SBT <24 hrs	Standard isocaloric	Days 1–4	382 ± 71 vs 1179 ± 338
1995	Hasse (33)	31	SBT <24 hrs vs oral	Standard isocaloric	Day 3	550 vs 1900
1996	Beier-Holgersen (34)	60	SBT <4 hrs	Nutrition supplement	Day 3 (median)	0 vs 1500
1996	Carr (35)	28	SBT <2 hrs	Standard isocaloric	Days 1–4	377 ± 34 vs 1622 ± 375
1997	Watters (36)	28	Jejun <2 hrs	Standard isocaloric	Day 3	0 vs 1500
1997	Heslin (37)	164	Jejun <24 hrs	Immune enhancing diet	Day 3, % goal	22% vs 58%
1997	Schilder (38)	94	Oral intake <24 hrs	Blenderized liquid diet	—	—
1998	Singh (39)	43	Jejun <12 hrs	Liquid diet	Day 4	406 ± 89 vs 2116 ± 243
Trauma						
1984	Seri (40)	18	Jejun <12 hrs	Blenderized liquid diet	—	—
1986	Moore (41)	63	Jejun <24 hrs	Elemental diet	Day 4, % goal	36 ± 2% vs 156 ± 11%
1998	Kompan (42)	28	OG <6 hrs	Standard isocaloric	Day 4	703 ± 701 vs 1340 ± 473
Head injury						
1989	Grahm (43)	32	SBT <36 hrs	Elemental diet	Day 3	411 vs 2499
1999	Taylor (44)	82	OG/SBT <24 hrs	Hypercaloric (1.5 kcal/mL)	Day 2, % of goal	20% vs 58%
Burns						
1990	Chiarelli (45)	20	<24 hrs	Blenderized liquid diet	—	—

SBT, small bowel tube; jejun, jejunostomy; OG, orogastric tube; —, data not available.

Table 2. Summary of outcomes data of studies included in meta-analysis

Date	Author	n	Study Protocol Control vs	Outcome Variables (Control vs Intervention)			
				Mean LOS (days)	Infections	Other Complications	Mortality
Abdominal surgery							
1979	Sagar (31)	30	SBT <24 hrs	19 vs 14	5/15 vs 3/15	—	—
1991	Schroeder (32)	32	SBT <24 hrs	15 vs 10	0/16 vs 1/16	7/16 vs 3/16	—
1995	Hasse (33)	31	SBT <24 hrs	18 vs 16	8/17 vs 3/14	—	—
1996	Beier-Holgersen (34)	60	SBT <4 hrs[a]	12 vs 8	14/30 vs 2/30	5/30 vs 6/30	4/30 vs 2/30
1996	Carr (35)	28	SBT <2 hrs	9 vs 10	3/14 vs 0/14	13/14 vs 3/14	1/14 vs 0/14
1997	Watters (36)	28	Jejun <2 hrs	16 vs 17	—	3/15 vs 3/13	—
1997	Heslin (37)	164	Jejun <24 hrs	—	6/83 vs 6/81	23/83 vs 31/81	—
1997	Schilder (38)	94	Oral intake <24 hrs	4 vs 3	—	—	—
1998	Singh (39)	43	Jejun <12 hrs	13 vs 15	22/22 vs 8/21	7/22 vs 8/21	4/22 vs 4/21
Trauma							
1984	Seri (40)	18	Jejun <12 hrs	—	2/8 vs 1/10	—	—
1986	Moore (41)	63	Jejun <24 hrs	29 vs 25	9/31 vs 3/32	15/31 vs 14/32	2/31 vs 1/32
1998	Kompan (42)	28	OG <6 hrs	14 vs 11	—	MOF 3.1 vs 2.5	—
Head injury							
1989	Grahm (43)	32	SBT <36 hrs	10 vs 7[b]	14/15 vs 3/17	—	—
1999	Taylor (44)	82	OG/SBT <24 hrs	—	35/41 vs 25/41	25/41 vs 15/41	6/41 vs 5/41
Burns							
1990	Chiarelli (45)	20	<24 hrs	89 vs 69	7/10 vs 3/10[c]	2/10 vs 2/10	0/10 vs 0/10

LOS, length of stay; SBT, small bowel tube; jejun, jejunostomy; MOF, multiple organ failure score.
[a]Double-blind, placebo-controlled randomized controlled trial.
[b]Intensive care unit LOS.
[c]Patients with bloodstream infection.

with study investigators being aware of treatment allocation. We believed the latter to be particularly important as blinding of the investigator(s) as to the timing of enteral nutrition is challenging. Only one of the studies included in this meta-analysis was placebo-controlled (34). Furthermore, the small size of most of the studies included in this meta-analysis and the different types of nutritional formulas used may have contributed to the differences in the treatment effect between studies. Differences in the underlying risk of patients have also been proposed as an explanation for the differences between the results of studies in a meta-analysis (58, 59). We were unable to control for risk (of infectious or

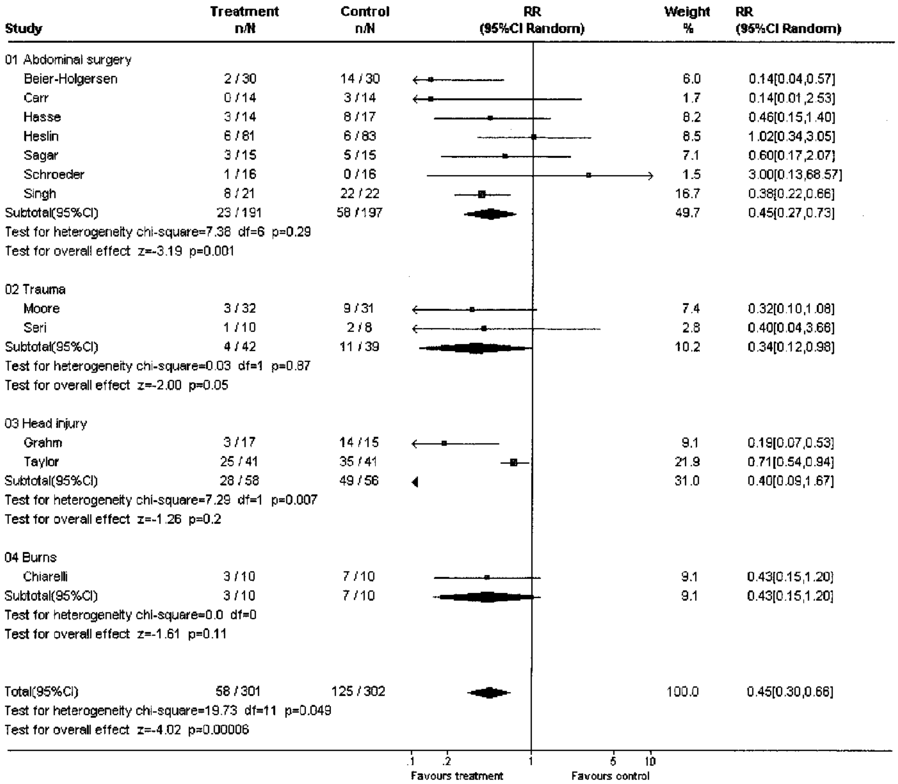

Figure 1. Random effects model of relative risk (*RR*) (95% confidence interval [*CI*]) of infectious complications associated with early enteral feeding compared with delayed feeding.

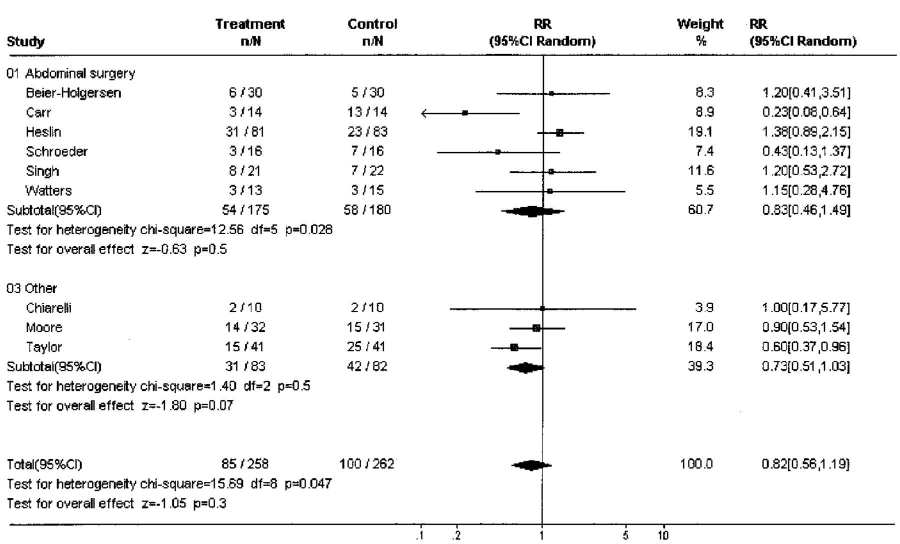

Figure 2. Random effects model of relative risk (*RR*) (95% confidence interval [*CI*]) of noninfectious complications associated with early enteral feeding compared with delayed feeding.

The results of our analysis of prospective, randomized clinical trials of early vs. delayed enteral nutritional support in critically ill patients indicate that early feeding decreases infectious complications and length of stay.

noninfectious complications) in this meta-analysis, but, considering the diversity of the patient populations, this factor may have contributed to the heterogeneity between studies. It is noteworthy that the test for heterogeneity just reached statistical significance for infectious complications ($p = .049$), whereas, it was highly significant for LOS ($p = .0012$); this would suggest that the early initiation of enteral nutrition may directly impact on infectious complications, but that many other factors may determine LOS. The results of this meta-analysis are comparable to those of Beale and colleagues (19), who demonstrated that an immune-enhancing diet compared with a standard enteral nutritional formula reduced infectious complications and LOS in critically ill patients, with no significant effect on mortality. Considering the complexity of critically ill patients and the multiple factors affecting outcome, only a mega-trial is likely to be able to demonstrate a significant difference in mortality between the early and delayed initiation of enteral nutrition; such a study would be almost impossible to perform (60).

Notwithstanding the limitations of this meta-analysis, the lower risk of infections and LOS in the early nutritional group is supported by findings from previous studies performed over the last two decades. Starvation is well known to cause immune depression and predispose to infections in humans. The effects of starvation are reversed by feeding. However, the benefits of immediate or early feeding after injury or illness compared with a few days' delay in feeding has remained controversial. The effects of nutrition on immune function and infection rates (10–19) led to the discovery of immune-enhancing nutrients and the development of "immune-enhancing" diets enriched in omega-3 long chain fatty acids, arginine, glutamine, nucleotides, and antioxidants. The immune-enhancing diets have been reported to decrease infection rates and improve outcome in critically ill patients (10–19). For example, Braga and colleagues (61) demonstrated that the perioperative administration of an enriched enteral formula significantly improved gut function and positively modulated postsurgical immunosuppressive and inflammatory responses compared

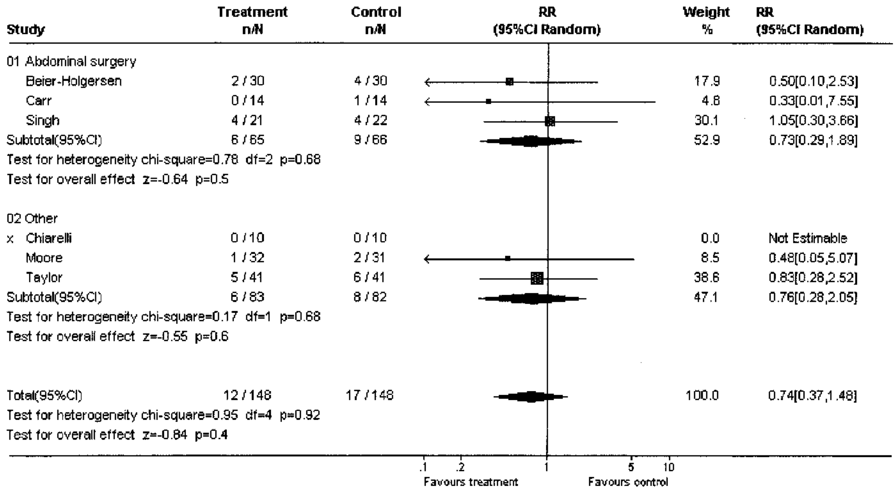

Figure 3. Random effects model of weighted mean difference (95% confidence interval [*CI*]) of length of stay associated with early enteral feeding compared with delayed feeding. *RR*, relative risk.

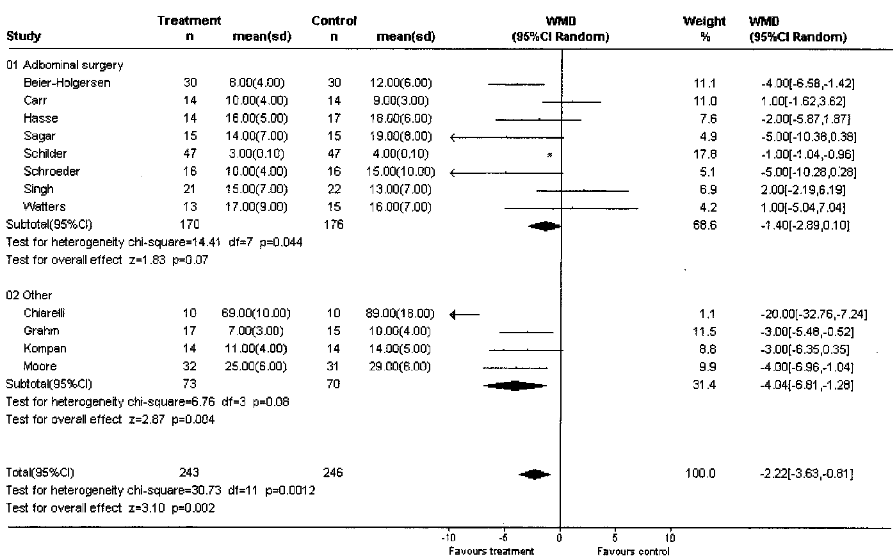

Figure 4. Random effects model of relative risk (95% confidence interval [*CI*]) of death associated with early enteral feeding compared with delayed feeding. *WMD*, weighted mean difference.

with a standard formula. Only one of the studies included in our analysis compared early with delayed feeding with an immune-enhancing diet (37). In an additional study, which did not meet our inclusion criteria, Kudsk et al. (54) compared early feeding with an immune-enhancing vs. standard enteral nutritional formula. However, the investigators also compared outcome in these fed patients with a separate group of similar patients who were not started on early nutritional support. The groups receiving early enteral nutrition had lower infection rates, complications, and LOS.

Early enteral feeding has been reported to improve organ function, which may explain the decreased hospital stay. In a number of landmark studies, Alexander and colleagues (25, 62–65) demonstrated that immediate enteral feeding in burned animals was associated with a decrease in the hypermetabolic state, lower levels of circulating stress hormones (i.e., glucagon, cortisol, and norepinephrine), increased gastrointestinal blood flow, a reduction in bacterial translocation from the intestinal tract, and improved outcome. Tanigawa et al. (27) demonstrated that feeding diminished lipid peroxidation during reperfusion after ischemia in the perfused rat liver. A number of studies demonstrate that starvation for as short as 12 hrs after injury depletes tissue antioxidant systems whereas early feeding after injury helps maintain tissue antioxidant levels (66–70). Zaloga and colleagues (28, 71) reported that early enteral feeding protected the liver from injury after hemorrhage and endotoxemia and the kidney from damage after rhabdomyolysis. Schroeder et al. (32) and Moss et al. (72) demonstrated that immediate postoperative enteral nutrition improved wound healing. Early enteral nutrition is known to improve protein synthesis (32, 73). Finally, Kompan and colleagues (42) demonstrated that enteral nutrition started within 6 hrs of admission to the ICU preserved intestinal permeability and was associated with a reduction in the incidence of organ failure when compared with trauma patients in whom enteral nutrition was started >24 hrs after admission.

All of the studies included in our analysis of early enteral nutrition were performed in surgical patients. We could find no studies that met our inclusion criteria that were performed in critically ill medical patients. This is clearly an area that requires additional study. However, we believe that medical patients would also receive benefits from early enteral feeding. In support of this statement, early feeding with immune-enhancing vs. standard enteral formulas benefits both surgical and medical critically ill patients (19). In addition, four studies performed in patients with hip fractures indicate that early nutritional support is associated with less complications, decreased hospital stay, and lower mortality (46–50).

The results of our analysis of prospective, randomized clinical trials of early vs. delayed enteral nutritional support in critically ill patients indicate that early feeding decreases infectious complications and LOS. The results of this meta-analysis must, however, be interpreted with some caution because of the significant heterogeneity between studies. A large, multicenter, prospective, double-blind, randomized study would provide more definitive evaluation of the benefits of early enteral feeding. However, until such a study is performed, current data supports the use of early enteral nutritional support in critically ill patients. The studies in this report did not evaluate the use of gastric vs. small-bowel feeding tubes for early feeding. Additional studies addressing the site of feeding would be of clinical value.

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A collective task force of the American College of Chest Physicians, American Association of Respiratory Care, and the Society of Critical Care Medicine have published "Evidence-Based Guidelines for Weaning and Discontinuing Ventilatory Support." They appear in the supplement to the December 2001 issue of *Chest*.

Nutrition in Burns: Galveston Contributions

Noe A. Rodriguez, Marc G. Jeschke, Felicia N. Williams, Lars-Peter Kamolz and David N. Herndon

Review

Nutrition in Burns: Galveston Contributions

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Aggressive nutrition support is recommended following severe burn injury. Initially, such injury results in a prolonged and persistent hypermetabolic response mediated by a 10- to 20-fold elevation in plasma catecholamines, cortisol, and inflammatory mediators. This response leads to twice-normal metabolic rates, whole-body catabolism, muscle wasting, and severe cachexia. Thus, it is relevant to review the literature on nutrition in burns to adjust/update treatment. Failure to meet the increased substrate requirements may result in impaired wound healing, multiorgan dysfunction, increased susceptibility to infection, and death. Therefore, aggressive nutrition support is essential to ensure adequate burn care, attenuate the hypermetabolic response, optimize wound healing, minimize devastating catabolism, and reduce morbidity and mortality. Here, the authors provide nutrition recommendations gained from prospective trials, retrospective analyses, and expert opinions based on the authors' practices in Galveston, Texas, and Vienna, Austria. (*JPEN J Parenter Enteral Nutr*. 2011;35:**704-714**)

Keywords: adult; pediatrics; burns; critical care; trauma; wound healing; enteral nutrition

Clinical Relevancy Statement

Provision of nutrition support is an essential component of burn care. Adequate assessment and management can reduce mortality and complications, optimize wound healing, and minimize the deleterious effects of the exaggerated hypermetabolic response; therefore, careful attention must be given to the tools and methods by which we estimate caloric needs. This review allows the reader to possibly change practice in burn nutrition. Furthermore, on the basis of the review data, we believe that that there should be discussion and thought about the ideal intensive care unit nutrition.

Introduction

Severe burn injury is associated with metabolic alterations that persist for up to 2 years postburn.[1] Immediately after injury, patients enter a period of attenuated metabolism and decreased tissue perfusion, also referred to as the "ebb" phase. Shortly after, they enter a phase of hypermetabolic rates and hyperdynamic circulation, known as the "flow" state.[2] The hypermetabolic phase is coordinated via mediators that initiate a cascade of metabolic alterations that can, in turn, prolong recovery or cause death. Management of this response can constitute a challenging endeavor to the surgeon, who is faced with the decision to implement myriad strategies that can include environmental thermoregulation, surgical excision and grafting, exercise, analgesia, anabolic hormones, and catecholamine antagonists. The global success of this effort, however, relies on the prompt commencement and maintenance of adequate nutrition support. We present recommendations gained from prospective trials, retrospective analyses, and expert opinions based on Galveston's contributions that we expect will aid in the nutrition assessment and management of severely burned adult and pediatric patients.

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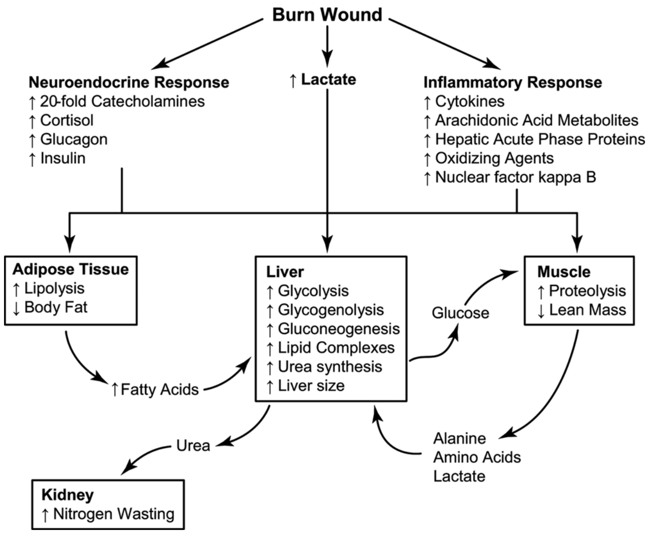

Figure 1. Metabolic response postburn. Severe burn injury leads to profound hypermetabolic response mediated by catecholamines, cortisol, and glucagon. Stress hormones lead to significant physiologic and metabolic derangements in every organ system. Reprinted with permission from *Annals Surgery*. 2008;248:387-401; Figure 1, Nutrition in Burns.

Prolonged and persistent hypercatabolism provokes a dreadful cascade of events, including weight loss, constitutive muscle and bone catabolism, growth retardation, immunosuppression, infection, physiologic exhaustion, and possible death.[3-5] A 10% loss of total body mass leads to immune dysfunction; 20%, to decreased wound healing; 30%, to severe infections; and 40%, to death.[6] In the past, severely burned, catabolic patients would routinely lose up to 25% of their total body mass. Even today, although rare, patients may still develop caloric deficits in the tens of thousands that translate into massive weight losses. The hypermetabolic and hypercatabolic response after severe burn injury requires an aggressive nutrition replacement.

Metabolic Response Postburn

The primary mediators of the hypermetabolic response postburn are catecholamines, corticosteroids, and inflammatory cytokines.[7,8] Burn patients show a 10- to 20-fold elevation in catecholamines and corticosteroid levels, which may last up to 12 months postburn and a considerably altered expression of acute and constitutive proteins that last up to 2 months postinjury.[8] These catabolic hormones thwart the action of insulin and establish a state of increased lipolysis, proteolysis, gluconeogenesis, and energy consumption (Figure 1). Plasma glucose and insulin levels increase and remain significantly elevated throughout the entire hospital stay.[8] On one hand, the moderately increased glucose availability is beneficial to supply the heightened energy demand, aiding muscle tissue with a "protein-sparing" effect that attenuates catabolism by reducing gluconeogenesis and amino acid oxidation.[8-10] Conversely, excessively high glucose levels can lead critically ill patients to poorer morbidity and mortality outcomes by increasing the risk for skin graft failure and wound infections.[9,11,12] The presence of vast numbers of inflammatory mediators adds to the multiple factors that make the nutrition management in burned patients an intricate task.

Burned children, in comparison to nonburned, have a significant and persistent increase in actual resting energy expenditure (REE) for up to 24 months postinjury. Their REE increases in a curvilinear fashion in relation to total body surface area (TBSA) burned. Thus, pediatric patients with ≤10% TBSA burns show close-to-normal percent predicted REE, and those with ≥40% TBSA burns may experience one and one-half normal percent predicted REE within the first 2 weeks postburn. It has been noted that at a neutral room temperature of 30°C, the metabolic rates of these patients approach 150% predicted REE and may decrease to 135% once the wounds have fully healed.[8] Not until 2 years postburn do patients approach metabolic rates of 110%–120% predicted REE, based on the Harris-Benedict equation.[1]

The obligatory state to supply fuel postburn allows muscle protein to be degraded much faster than it is synthesized,[8,13] causing net loss of protein soon after burn. Sustained losses lead to a decrease in lean body mass, severe muscle wasting, and failure to fully rehabilitate. The protein loss is directly related to increases in metabolic rate and may persist for up to 24 months postburn, often resulting in significantly negative whole-body and cross-leg nitrogen balances.[14-16] Severely burned patients have a nitrogen loss of 20–25 g/m^2 TBSA/d,[15] which—if unattended—results in lethal cachexia in <30 days. In young children, protein loss leads to significant growth retardation for >1 year postinjury.[17]

Data obtained by stable isotope techniques reveal the significant derangements in protein turnover, urea production, and gluconeogenesis in burned patients. During the postburn hypermetabolic response, both glycolytic-gluconeogenic and triglyceride–fatty acid cycling have been reported to increase by 250% and 450%, respectively.[5,18] Collectively, these changes increase glycogenolysis, gluconeogenesis, and circulation of glucogenic precursors, which translate into hyperglycemia and impaired insulin responsiveness, in turn related to postreceptor insulin resistance.[4] Although glucose delivery to peripheral tissues is increased by up to 3-fold, glucose oxidation is restricted, leading to elevated fasting glucose. Increased glucose production is directed, in part, to the burn wound to support the anaerobic metabolism of

fibroblasts, endothelial cells, and inflammatory cells.[19] Following excessive endogenous lipolysis, the liver increases its size by 225% of normal by 2 weeks postburn[18] and remains increased at discharge by 200%.[8,20] The end product of anaerobic glucose oxidation—lactate—is recycled to the liver to produce more glucose via gluconeogenic pathways.[15] Adequate nutrition support is an effective nonpharmacological strategy to attenuate these catastrophic metabolic responses.

Timing of Nutrition

Advances in burn care altered the magnitude of the postburn hypermetabolic response but not the nature of the response.[21] A major determinant of outcome for severe burn patients is time to treatment. Any delays in resuscitation lead to poorer outcomes.[22] Acutely, there is significant gut mucosal damage and increased bacterial translocation that collectively lead to decreased nutrient absorption.[23,24] As such, optimal nutrition support for the severely burned patient is best accomplished by early (within 24 hours after injury) initiation of enteral nutrition (EN).[25] Multiple studies demonstrate that the early institution of enteral feeding can significantly modulate the hypermetabolic response to severe burn.[26] Animal studies showed significant decreases in metabolic rates by 2 weeks postburn in animals enterally fed continuously by 2 hours postburn compared to animals fed 3 days postburn, indicating the benefits of early initiation. There is significant modulation of catecholamine levels and support of gut mucosal integrity with early EN.[27]

In human studies, early and continuous EN has been shown to effectively deliver caloric requirements (REE) by postburn day 3, diminish the hypermetabolic response, and decrease circulating levels of catecholamines, cortisol, and glucagon.[27,28] Early EN also preserves gut mucosal integrity, motility, and intestinal blood flow, which are important to prevent intestinal hypoperfusion or ileus due to delays in resuscitation or reperfusion. Because the postburn ileus primarily affects the stomach and colon,[29] patients with severe burn injury can be fed through enteral tubes to the small bowel (duodenum or jejunum) 6 hours postburn, independently of total gastroduodenal function.[30]

Nutrition Assessment and Monitoring

Optimal nutrition assessment of the burned patient should comprise a complete review of the features in the history and physical exam that may affect nutrition management. These commonly include preexisting malnutrition, malabsorption, paralytic ileus, severe short bowel syndrome, and presence of severe shock, obstruction, or diffuse peritonitis. Additional laboratory, clinical, and metabolic examinations are not only recommended for the initial assessment but for the continued monitoring postburn. Serum proteins, nitrogen balance, anthropometric measurements, intake and output of fluids, indirect calorimetry, and tests of immune function are methods that provide a fair overview of the metabolic alterations in the postburn period. In the majority of surgical specialties, perioperative levels of serum albumin are better predictors of morbidity and mortality than other biochemical markers and even anthropomorphic measurements.[31,32] Patients with serum albumin levels at a cutoff point of 21 g/L present a 30% increased risk of 30-day mortality and up to 65% risk of 30-day morbidity. However, in burned patients, weekly levels of serum prealbumin (transthyretin) are a better nutrition marker than albumin. Prealbumin levels show a maximal decrease between days 6 and 8 in all burned patients, but persistent low levels (100–150 mg/L on days 14–17 postburn) are associated with a decreased likelihood of survival.[33,34] Even when patients do survive, persistently low prealbumin values are associated with a higher incidence of sepsis, lengthier stays, and a decreased ability for wound healing.[33,34] Notably, prealbumin levels are inversely correlated to increased acute-phase protein levels (ie, C-reactive protein). Prealbumin, as opposed to albumin, can also be used as a sensitive tool in predicting graft take in burned patients.[35]

Nutrition assessment in burned children should include plotting of the patient's height and weight on percentile charts. The Centers for Disease Control and Prevention (CDC) has published revised standard gender-specific percentile charts that provide data on height for age, weight for age and body mass index (BMI). These charts are demographically representative of the U.S. population for ages 2–20 years, with charts also available for younger children. In the acute setting, these charts allow evaluation of the nutrition status of patients whose nutrition history is limited. A BMI below the 5th percentile indicates an underweight patient, whereas a trend line crossing 2 major percentile lines signifies a growth problem or failure to thrive. In the postacute setting, these charts are used to monitor the patient's long-term nutrition status. It should be noted that fluid overload not uncommonly masks a continuing loss of lean body mass. Thus, such patients can suffer significant inanition and still weigh more than at the time of admission. In addition, fluid shifts associated with infections, ventilator support, hypoproteinemia, and elevations in aldosterone and antidiuretic hormone lead to wide fluctuations in weight that have little to do with nutrition status.[36] Judicious monitoring of weight trends should be a priority in the clinical management of severely burned patients. Although no single laboratory test is fully reliable in nutrition monitoring, systematic and holistic assessments are key to management of the ever-evolving physiologic response postburn.

Table 1. Equations Used to Estimate Caloric Requirements in Burned Patients

Age, y	Formula Name	Formula
0–1	Galveston Infant	2100 kcal/m² + 1000 kcal/m² burn
1–11	Galveston Revised	1800 kcal/m² + 1300 kcal/m² burn
12–16	Galveston Adolescent	1500 kcal/m² + 1500 kcal/m² burn
16–59	Curreri Formula	25 kcal/kg of weight + (40) TBSA
	Toronto Formula	−4343 + (10.5 × TBSA) + (0.23 × CI) + (0.84 × HBE) + (114 × T) – (4.5 × PBD)
≥60	Curreri Formula	20 kcal/kg of weight + (65) TBSA

Resting energy expenditure (REE) measurements are used to guide nutrition management. Corrected 1.2–1.4× measured REE kcal/d is recommended for patients ≥3 years of age. CI, total calorie intake the previous day; HBE, Harris-Benedict estimates; PBD, number of postburn days to the day preceding the estimation; T, average of core temperatures (°C) the previous day; TBSA, burn size (percent total body surface area).

Addressing Caloric Requirements

As part of our routine clinical practice, indirect calorimetry is performed in all patients between midnight and 5 AM while asleep. Measured resting energy expenditure (MREE) is determined within 1 week of admission and weekly thereafter during their acute hospitalization. Actual MREE is expressed in units of kcal/d and is used to guide nutrition management and to estimate caloric requirements. Predicted REE, as expressed by MREE/predicted basal metabolic rate from the Harris-Benedict equation, is used as an indicator of the degree of hypermetabolism. Mlcak et al[37] stratified indirect calorimetry data of pediatric burn patients (n = 100) by gender and showed that males exert predicted REE 10–20 percentage points higher than females, a significant difference that last up to 9 months postburn. Stratification in 3 age groups representing children <3, 3–9.9, and 10–18 years of age showed predicted REEs of 118% ± 10%, 139% ± 7%, and 152% ± 6%, respectively. A significant difference was shown only between the former and latter groups. In adult burn patients (≥20% TBSA burned), current reports indicate higher predicted REEs with an average of 160% and a standard deviation up to 30%.[38,39]

Considering the high cost of acquiring and maintaining the equipment for bedside indirect calorimetry, more centers have adapted predictive historical equations to estimate caloric requirements in burn patients. Through elaborate formulas, patient-specific factors such as age, gender, weight, temperature, and burn size are collected on a day-to-day basis to estimate caloric needs. Historically, however, adapted equations in common use such as Curreri, Harris-Benedict, Schofield-HW, and World Health Organization, have overpredicted basal metabolic rates, resulting in increased risk of overfeeding and adverse events.[40,41] Not surprisingly, lack of a correcting factor in nonadapted formulas underestimates caloric needs. The adapted Toronto formula is an exception. It correlates well with MREE (r^2 = 0.67) but is complicated to use.[38] Studies have shown that MREE requires a correcting factor of 30% to maintain adequate body weight, obtained by the product of a 1.2–1.4 factor.[41-44] The rationale for the alluded factor comes from the intention of measuring total energy expenditure (TEE), which represents the most direct assessment of caloric requirements. TEE measurement, however, requires application of a doubly labeled water technique that is invasive and not feasible for routine use. As shown by Goran et al,[45] TEE assessed by this technique was significantly correlated with 1.18 ± 0.17 times MREE (r^2 = 0.92) from indirect calorimetry. In other words, by supplementing 1.2× MREE kcal/d, a very close approximation to actual TEE is expected. Observational studies have shown an increase in body weight by feeding >1.4× MREE kcal/d; the gains however, were in fat deposition and thus not advocated.[41,42]

Ideally, optimal caloric balance should be determined from a prospective trial. Such a trial would include measures of morbidity and of functional outcome. Preservation of lean body mass should be a goal of nutrition support for severe burn victims because a major consequence of the hypermetabolic response is severe catabolism. It is our hope for the future that through further testing of these formulas and indirect calorimetry itself, an ideal method will be refined to optimally quantify requirements of nutrition support in burned children and adults. In line with above, in the treatment of severe burns, we advocate the use of indirect calorimetry to help guide caloric requirements estimated by common predictive equations (Table 1).

Substrate Requirements

Carbohydrates

Carbohydrates aid as fuel in wound healing and provide a protein-sparing effect that decreases the loss of lean body mass. Therefore, to adequately feed burned patients, one should first consider the minimum baseline adult requirements of carbohydrates (2 g/kg/d)[46] and the maximum

rate at which glucose can be assimilated in severely burned patients (7 g/kg/d).[47-49] These are important values that one should keep in mind in the management of hypermetabolic patients, as they occasionally have caloric requirements that can exceed the maximum rate at which the body is able to oxidize glucose.[47] In other words, severely burned patients may very well have greater needs than those that can safely be supplied. Inadequate carbohydrate delivery that fails to meet the increased demands of burned patients may lead to uncontrolled protein catabolism, whereas supplementation in excess of utilization leads to hyperglycemia, conversion of glucose into fat, glucosuria, polyuria, dehydration, and respiratory problems.

Adequate control of carbohydrate levels in critically ill patients usually goes hand in hand with watchful administration of anabolic hormones. Insulin therapy in burned patients stimulates muscle protein synthesis, increases lean body mass, and is associated with improved wound healing, without increasing hepatic triglyceride production.[50,51] Severely burned patients demonstrated improved donor site wound healing after receiving 7 days of continuous infusions of insulin and glucose titrated to maintain euglycemia and plasma insulin concentrations of 400–900 μU/mL.[52] In addition, patients receiving a high-carbohydrate, high-protein enteral formula and insulin infused at 1.5 μU/kg/min to maintain blood glucose levels between 100 and 140 mg/dL significantly improved lean body mass, bone mineral density, and decreased length of stay during the acute hospitalization.[53] Insulin therapy, however, may also lead to hypoglycemia in some patients and should be closely monitored as hypoglycemia can quickly lead to increased morbidity and mortality.

Fats

The administration of small amounts of dietary fat (ie, 2%–3% of linoleic acid) is critical to prevent the development of essential fatty acid deficiency.[54] In burned patients, the ability of the body to handle additional amounts of fat is significantly altered; thus, one should cautiously estimate the proportion of fat to be supplemented in nutrition protocols. Immediately after injury, there is an increase in peripheral fat breakdown, as well as in utilization of fat by the liver. Although, the increased β-oxidation of fat provides fuel during the hypermetabolic response, only 30% of the available free fatty acids undergo degradation; the rest undergoes reesterification and potential accumulation in the liver.[54]

Therefore, in burned patients, the percentage of dietary fat calories needs to be carefully considered. In our institution, we prefer EN specialty formulas with a very low fat content of 3%–15% of total calories. In patients receiving short-term (<10 days) parenteral nutrition (PN), we usually withhold entirely from using lipid emulsions.[55] For patients needing longer PN periods (>10 days), we use 0.5–1 g fat/kg/d, withholding administration to once or twice weekly based on individual assessment of benefits and safety.[56] In addition, the total number of nondietary fat calories is also to be considered. For example, propofol affects the total amount of fat calories administered in a given day. A 1% propofol solution has the same caloric value of a 10% intralipid emulsion (1.1 kcal/mL, 440 kcal in a 400-mL infusion) and may lead to significant metabolic alterations. Thus, serum triglyceride concentrations should be monitored in patients receiving such infusions and caloric intake corrected accordingly. One should also consider the types of dietary fat administered, as these are potentially as important as their amounts. Although there are insufficient data to decisively recommend the use of diets enriched with nutrients such as arginine and ω-3 fatty acids, some have suggested that patients with >30% TBSA third-degree burns may benefit from their use.[57] Common lipid sources high in ω-6 fatty acids are metabolized to proinflammatory cytokines, which may facilitate inflammation. In contrast, diets high in ω-3 fatty acids have been associated with improved outcomes, attenuated inflammatory response, and reduced incidence of hyperglycemia.[58-60]

Protein

After severe burns, proteolysis is a hallmark of the hypermetabolic response and can exceed 150 g/d or almost one-half pound of skeletal muscle.[61] These patients can oxidize amino acids at rates 50% higher than those seen in healthy fasting individuals. Such high breakdown rates frequently translate into significant loss of lean body mass, decreased wound healing, and immune incompetence. Therefore, attenuation of this response should be a goal of any nutrition, pharmacological, and nonpharmacological treatment regimens designed for burn patients.

Although the mechanism by which protein breakdown occurs is not yet fully understood, the human body is capable of sparing protein when adequately and timely supplemented with high-quality protein and carbohydrate. Comparably, if the amounts of supplemented protein are proportionally larger than the capacity of the protein pool in the body, increased urea production without improvements in lean body mass is anticipated.[62] In clinical practice, well-accepted protein requirements are estimated at 0.8–1 g/kg/d in healthy individuals,[63] at 1.5–2 g/kg/d in burned adults, and at 2.5–4.0 g/kg/d in burned children.[21,64,65] Undoubtedly, even at these relatively high replacement rates, it is not rare to encounter burned patients whose neuroendocrine and proinflammatory responses lead them to persisting loss of muscle protein.

Certain amino acids have a key role in recovery following injury. Severe burn increases skeletal muscle and

Table 2. Reference Daily Intake (RDI): Vitamin and Trace Elements Requirements[a]

Age, y	Vitamin A, IU	Vitamin D, IU	Vitamin E, IU	Vitamin C, mg	Vitamin K, mcg	Folate, mcg	Cu, mg	Fe, mg	Se, mcg	Zn, mg
0–13										
Nonburned	1300–2000	600	6–16	15–50	2–60	65–300	0.2–0.7	0.3–8	15–40	2–8
Burned	2500–5000			250–500		1000[b]	0.8–2.8		60–140	12.5–25
≥13 (includes adults)										
Nonburned	2000–3000	600	23	75–90	75–120	300–400	0.9	8–18	40–60	8–11
Burned	10,000			1000		1000[b]	4.0		300–500	25–40

RDI, Reference Daily Intake refers to the daily intake level that a healthy person should achieve. Conversion based on 1 mcg of vitamin A = 3.33 IU of vitamin A; 1 mcg of calciferol = 40 IU of vitamin D; 1 mg of α-tocopherol = 1.5 IU of vitamin E.

[a]Sources: Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride (1977); Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline (1988); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); and Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001). These reports may be accessed at http://www.nap.edu.

[b]Administered Monday, Wednesday, and Friday.

organ efflux of alanine (ALA), arginine (ARG), and glutamine (GLN). Available amino acids aid wound healing and supply energy to the liver[66]; GLN serves as a primary fuel in enterocytes and lymphocytes and plays a role maintaining small bowel integrity, preserving gut-associated immune function, and limiting intestinal permeability.[67-69] Low GLN plasma concentrations have been associated with an immunodeficient state, a propensity to infection, and an increased bowel permeability. Prospective, randomized studies conducted in burned adults have shown that supplementation of EN with GLN (0.35–0.57 g L-GLN/kg of body weight/d) either intravenously or via the gastrointestinal (GI) tract is associated with decreased incidence of infections, improved visceral protein levels, decreased length of stay, and reduced mortality.[69,70]

Vitamins and Trace Elements

After burn injury, patients enter a period marked by extensive loss of tissue, altered metabolism, increased inflammation, and distorted cell membrane homeostasis. These, combined with a substantial redistribution of fluid and nutrients, sets the stage for the development of vitamin deficiencies and a long-lasting oxidant/antioxidant imbalance proportional to the severity of the burn.[71-73] Decreased levels of vitamins A, C, and D and trace elements such as Fe, Cu, Se, and Zn have been shown to adversely affect wound healing and skeletal, neuromuscular, and immune system function.[72,74] Subsequently, oxidative stress also contributes to secondary tissue damage and further impairs the immune function. Prompt replacement of vitamins is recommended. Vitamin A improves wound healing time due to an effect in epithelial growth, whereas vitamin C facilitates synthesis and cross-linking of collagen.[72,75] Daily recommended intakes for vitamins A and C are listed in Table 2. The exact role of vitamin D deficiency in failure of bone density to reach that of nonburned peers is unknown.[76] In a recent study, severely burned children were discharged on a multivitamin containing 400 IU of vitamin D_2; serum levels of 25-hydroxyvitamin D were monitored. After 6 months, vitamin D insufficiency remained evident in all but 1 of the 8 patients studied. This finding suggests that the exact vitamin D requirement following burn injury also remains unknown.[77]

Trace elements (Fe, Cu, Se, and Zn) are involved in humoral and cellular immunity.[74,78] Fe is an important cofactor in oxygen-carrying proteins.[21] Zn plays a role in wound healing, DNA replication, lymphocyte function, and protein synthesis.[79] Se improves cell-mediated immunity and activates the nuclear transcription factor NF-κB.[74,80] Cu is necessary for collagen synthesis and wound healing. Deficiencies in Cu have been linked to fatal arrhythmias, altered immunity, and poorer outcomes.[74,81] Plasma levels of these trace elements are significantly depressed for prolonged periods after the acute injury due to increased urinary excretion and significant cutaneous losses.[82-85] Collectively, replacement of all these micronutrients has been found to contribute to the improvement in morbidity of severely burned patients.[86-88] Daily use of multivitamins provides the recommended daily averages estimated for healthy individuals; however, further studies in burned patients are necessary to determine doses required to reach desired plasma levels (Table 3).

Routes of Nutrition Support

Severely burned patients who become victims of inanition generally succumb to severe systemic infections or respiratory failure.[89] Therefore, in the treatment of severe burns, major determining factors of success are the

Table 3. Selected Presentations of Vitamin and Trace Elements—Available in the United States

Age, y	Enteral		Parenteral	
0–12				
	Enfamil Poly-Vi Sol (1 mL)		**MVI Pediatric (5-mL vial)**	
	Vitamin A: 1500 IU	Vitamin D: 400 IU	Vitamin A: 2300 IU	Vitamin D: 10 mcg
	Vitamin C: 35 mg	Vitamin E: 5 IU	Vitamin C: 80 mg	Vitamin E: 7 mg
			Folate: 140 mcg	Vitamin K_1: 200 mcg
	Vitamin A: <2 y, 2500 IU		**Multitrace—4 Pediatric (3 ml vial)**	
	2–12 y, 5000 IU		Each mL provides:	
	Vitamin C: 250 mg		Zinc: 1 mg	Manganese: 25 mcg
	Vitamin E: 5 mg		Copper: 0.1 mg	Chromium: 1 mcg
	Folic acid: 1 mg[a]		**Selenium (sodium selenite—10 mcg/mL)**	
	Zinc sulfate: 50–110 mg			
≥12				
	Rx Choice Thera-Plus (5 mL)		**Infuvite Adult (5-mL vial)**	
	Vitamin A: 5000 IU	Vitamin D: 400 IU	Vitamin A: 3300 IU	Vitamin D: 200 IU
	Vitamin C: 35 mg		Vitamin C: 200 mg	Vitamin E: 10 IU
			Folate: 600 mg	Vitamin K_1: 150 mcg
	Folic acid: 1 mg[a]		**Multitrace—4 (10-mL vial)**	Each mL provides:
	Vitamin A: 10,000 IU		Zinc: 1 mg	Manganese: 100 mcg
			Copper: 0.4 mg	Chromium: 4 mcg
	Vitamin E: 10 mg		**Selenium (sodium selenite—10 mcg/mL)**	
	Zinc sulfate: 200 mg			

IU, International Units; mcg, micrograms; mg, milligrams; mL, milliliters.
[a]Administered Monday, Wednesday, and Friday.

installation of an adequate nutrition route and a subsequent nutrition regimen. Nutrition methods that involve oral alimentation are often unsustainable because of the frequency of altered mental status, inhalation injuries, endotracheal intubation, GI dysfunction, and feeding intolerance seen in burned patients. Even in absence of these factors, studies have shown that the use of oral alimentation alone is not ideal, as it can allow patients with 40% TBSA burns to lose up to a quarter of their preadmission weight by 21 days postinjury. Oral feedings in severely burned patients are also difficult to sustain because of the large and often intolerable amounts of food necessary to manage severe catabolism.

EN is a sensible, safe, cost-effective, and widely available feeding route; it has considerably improved outcomes by mitigating the degree of catabolism. EN offers a feasible route for early installation and maintenance of nutrition support in burn patients and several other forms of trauma.[26,90] EN maintains the structural and functional integrity of the gut, stimulates blood flow, and preserves first-pass nutrient delivery to the liver.[90] EN reduces translocation-bacteremia and sepsis, decreases the incidence of pneumonia and central line infections, and supports IgA production in the gut-associated immunocytes.[91,92] A multicenter study seeking to evaluate compliance of "early" (<24 hours from admission) installation of EN in adult burn patients (n = 153) found no significant difference in rates of hyperglycemia, abdominal compartment syndrome, or GI bleeding, but they exhibited shorter intensive care unit (ICU) length of stay (adjusted hazard ratio [HR] = 0.57; P = .03; 95% confidence interval [CI], 0.35–0.94) and reduced risk to develop wound infection (adjusted odds ratio [OR] = 0.28; P = .01; 95% CI, 0.10–0.76). Initiation of EN by 24 hours from admission is recommended as standard of care for severe burns.[93]

PN for the management of severe burns surfaced in the 1970s with the expectation that it would become standard of care. In the late 1980s, studies showed that use of PN, either alone or in combination with EN, was associated with overfeeding. Evident in these studies were increased incidence of liver malfunction, impaired immune response as seen by lower T cell helper/suppressor cell ratios, and heightened mortality by almost 3-fold.[94,95] These factors, combined with the incidence of mechanical and infectious complications of catheters, the increase in proinflammatory cytokines, and worsening of the pulmonary function, led to further deterrence from the use of PN in the early postburn period. Nonetheless, although current practice is to preferentially use the GI tract for nutrition support, the parenteral route can be used in burned patients whose caloric requirements cannot be supplied via EN. The question of whether we should initiate PN in the first 24 hours if EN is contraindicated stands unanswered; insight can be obtained from available evidence, but a definitive recommendation will need to be further evaluated. In a large meta-analysis conducted in critically ill patients that included a small number of burned patients, a grade B evidence-based

Table 4. Selected Enteral Nutrition Options for Burned Patients: U.S. Market

Nutrition	kcal/mL	CHO, g/L (% Cal)	PRO, g/L (% Cal)	Fat, g/L (% Cal)	Comments
Pediatric					
Vivonex RTF	1	175 (70)	50 (20)	12 (10)	Transitional feeding, low fat, high CHO, easily digestible
Vivonex TEN	1	210 (82)	38 (15)	2.8 (3)	Free AA, very low fat, high CHO.[98] Severe trauma or surgery.
Impact Glutamine	1.3	150 (46)	78 (24)	43 (30)	Immunonutrition, GLN, ARG, ω-3 fatty acids
Elecare	0.67	72 (43)	20 (15)	32 (42)	Prepared at 9.4 g/60 mL, AA-based nutrition
Adult					
Crucial	1.5	89 (36)	63 (25)	45 (39)	Immune enhancing with ARG, concentrated
Impact	1.0	130 (53)	56 (22)	28 (25)	Immune enhancing with ARG, GLN, fiber
Oxepa	1.5	105 (28)	63 (17)	94 (55)	ALI, ARDS period (2 wk),[60] concentrated
Glucerna	1.0	96 (34)	42 (17)	54 (49)	For glucose intolerant or diabetic patients, low CHO
Nepro	1.8	167 (34)	81 (18)	96 (48)	For CKD and patients on dialysis, concentrated
Osmolite 1 Cal	1.06	144 (54)	44 (17)	35 (29)	Isotonic, for use in intolerance to hyperosmolar nutrition
Modular (Children/Adult)					
Benefiber Powder	0.27	66 (100)			(Prepared at 4 g/60 mL) Tasteless, odorless, soluble fiber
Beneprotein	0.83		200 (100)		(Prepared at 7 g/30 mL) Whey protein, mixed in foods

AA, amino acid; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ARG, arginine; CHO, carbohydrate; CKD, chronic kidney disease; GLN, glutamine; PRO, protein. Data extrapolated from "Enteral Product Reference Guide, by Nestle Clinical Nutrition 2010" (Minneapolis, MN) and "Abbott Nutrition Pocket Guide © 2010."

recommendation has been made for the use of PN in patients in whom EN cannot be started within the first 24 hours of admission. A modified subgroup analysis attributed a reduction in risk of mortality to trials comparing PN to delayed (>24 hours) EN, despite an association with increased infectious complications with PN.[96,97] Studies specifically designed to evaluate this hypothesis in burned patients are necessary, and careful choosing of an equation to estimate caloric needs as well as the use of indirect calorimetry to guide nutrition is warranted.

Formulas

Milk became the standard of care for burn patients in the 1970s. In general, milk (44% fat, 42% carbohydrate, and 14% protein) was fairly well tolerated; however, it was considered a fat-based diet, which in certain clinical conditions did not seem to be the optimal source of energy. In the decades to follow, a debate about the roles of high-fat and high-carbohydrate diets in the care of critically ill patients was originated. In a prospective, randomized, crossover trial conducted on severely burned pediatric patients (n = 14), 2 isocaloric isnonitrogenous diets were examined, including a fat-based diet and a carbohydrate-based diet. Cross-leg stable isotope techniques detected that patients on high-carbohydrate regimens (3% fat, 15% protein, and 82% carbohydrate) had improved muscle catabolism, suggestive of a protein-sparing effect associated with higher endogenous insulin concentrations.[98] When this study was published, it was suggested that high-carbohydrate diets in critically ill adults may result in hyperglycemia and may have no effect on protein metabolism.[99] A prospective, randomized, multicenter trial in critically ill adults (n = 47), later examined 2 PN dietary regimens, one with a glucose/lipid ratio of 80/20 (high-carbohydrate) and the other with a 50/50 (high-fat) ratio. It was determined that the high-carbohydrate regimen had a better nitrogen-sparing effect but at the risk of altered glycemic control.[100] Although this study included only 2 burned adults, a reasonable recommendation is that in acutely ill burn patients, regardless of age, a high-carbohydrate diet is preferred (Table 4).

Immune-enhancing formulas consist of macronutrients enriched with arginine, glutamine, nucleotides, and ω-3 fatty acids. These nutrition regimens have shown to be beneficial in nonburned patients in terms of neutrophil recruitment, respiratory gas exchange, cardiopulmonary function, days on mechanical ventilation, and length of hospital stay. However, little is known about their effect in burn patients. A recent report examining 19 burned pediatric patients showed a benefit resulting from the use of an ω-3 fatty acid–based diet in patients with acute lung injury or acute respiratory distress syndrome. The use of a high-fat concentrated formula (55% fat, 17% protein, and 28% carbohydrate) enriched with eicosapentaenoic acid showed

to be safe and well tolerated, and it may have a role improving oxygenation and pulmonary compliance.[60] Nevertheless, applicability of these findings is not recommended until prospective studies have been conducted. If such studies were to be conducted, careful attention should be rendered to the liver, where a high-fat diet may be deleterious.

Single-macronutrient formulas consist of either fiber or protein as the main source of energy. Protein is supplemented to standard or specialty formulas in clinical scenarios marked by severe loss of muscle mass and immunodeficiency, whereas fiber is added in the event of constipation, aiding to normalize bowel function. Whole-protein formulations are appropriate in most patients; peptide-based or free amino acid formulations may be considered in patients with a severely compromised GI tract or severe protein/fat malabsorption. Considering that many formulas are hyperosmolar at full strength, dilution by one-fourth to one-half is initially preferred to minimize the possibility of diarrhea from excess osmotic load and to facilitate absorption.

PN formulas, in the United States, are composed from a 70% dextrose (D70) solution, 10%–20% amino acid solutions, and 10%–20% lipid emulsions. These formulas can be individually adjusted to meet the patients' needs for the intake of calories, electrolytes, vitamins, and trace elements and administered with medications such as insulin and H_2 blockers.

Complications

Overfeeding of burned patients can lead to major complications. For example, carbohydrate overfeeding may result in elevated respiratory quotients, increased fat synthesis, and increased CO_2 elimination. Moreover, overfed ventilated patients become more difficult to manage or wean from ventilator support.[101] Excess carbohydrate or fat can also lead to fat deposition in the liver[102] and excess protein replacement to elevations in serum urea nitrogen.[102] In addition, overfeeding can augment hyperglycemia, which can be difficult to treat, as both endogenous and exogenous insulin effects are often countered by the surge of catabolic hormones.[103] Finally, attempting to overcompensate by providing excess calories and/or protein is ineffective and likely to increase complications such as hyperglycemia, CO_2 retention, and azotemia.[21] These complications are not specific to parenteral or enteral feedings but are instead due to overcompensating for the remarkably increased substrate demand experienced by burned patients.

Summary

Severe burns increase nutrition requirements because of the prolonged hypermetabolic, hypercatabolic response, which may lead to loss of lean body mass and poor outcomes. Although multiple treatment strategies have contributed to the improvements in morbidity and mortality of these patients, they have not proved sufficient to completely abate the response postinjury. Among these strategies, EN is safe, widely available, and effective in decreasing loss of lean body mass.[8,104] More important, EN is beneficial in restoring and maintaining intestinal tract integrity and functionality. Therefore, it should be initiated early after admission and followed by judicious assessment and monitoring of the patients' nutrition status. As patients recover after injury, they present multiple physiological changes that make the task of nutrition assessment rather intricate. Research involving dual-energy X-ray absorptiometry, electrical bioimpedance, and indirect calorimetry allows us to determine if particular changes in weight are nutritionally significant and to evaluate if the course of action followed attained the nutrition objectives.

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